PCT

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : G06F 15/42

A1

(11) International Publication Number: WO 94/11837

(43) International Publication Date: 26 May 1994 (26.05.94)

(21) International Application Number: PCT/US93/10507

(22) International Filing Date: 8 November 1993 (08.11.93)

(30) Priority data:
07/975,526 12 November 1992 (12.11.92) US

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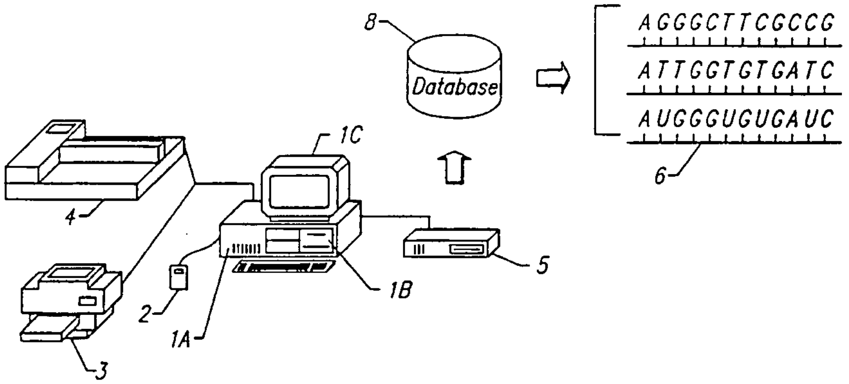
(81) Designated States: CA, DE, GB, JP, KR, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
With amended claims.

(54) Title: OLIGOPROBE DESIGNSTATIONS: A COMPUTERIZED METHOD FOR DESIGNING OPTIMAL OLIGONUCLEOTIDE PROBES AND PRIMERS



(57) Abstract

There is disclosed herein an invention which relates to the fields of genetic engineering, microbiology, and computer science, that allows a user, whether a molecular biologist or a clinical diagnostician, to calculate and design extremely specific oligonucleotide sequences for DNA and mRNA hybridization procedures. The sequences designed with this invention may be used for medical diagnostic kits, DNA indentification, and potentially continuous monitoring of metabolic processes in human beings. The key features design oligonucleotide sequences based on the GenBank database of DNA and mRNA sequences and examine candidate sequences for specificity or commonality with respect to a user-selected experimental preparation. Two models are available: a Mismatch Model, that employs hashing and continuous seed filtration, and an H-site Model, that analyzes candidate sequences for their binding specificity relative to some known set of mRNA or DNA sequences. The preferred embodiment of this computerized design tool is written in the Borland R C++ language and runs under Microsoft R Windows TM on IBM R compatible personal computers.

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OLIGOPROBE DESIGNSTATION: A COMPUTERIZED METHOD FOR DESIGNING OPTIMAL OLIGONUCLEOTIDE PROBES AND PRIMERS

BACKGROUND OF THE INVENTION

This invention relates to the fields of genetic engineering, microbiology, and computer science, and more specifically to an invention that helps the user, whether they be a molecular biologist or a clinical diagnostician, to calculate and design extremely accurate oligonucleotide sequences for use as probes, for example for DNA and mRNA hybridization procedures, or as primers, for example for DNA amplification and extension using the polymerase chain reaction (PCR). In the following description, the design of probes has been discussed.

The oligonucleotide probes designed with this invention may be used to test for the presence of precursors of specific proteins in living tissues, or may be used for medical diagnostic kits, DNA identification, and potentially continuous monitoring of metabolic processes in human beings. The present implementation of this computerized design tool runs under Microsoft® Windows™ v. 3.1 (made by Microsoft Corporation of Redmond, Washington) on IBM® compatible personal computers (PC's).

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are now described. All publications mentioned hereunder are incorporated herein by reference.

To isolate a specific gene for any particular purpose, a researcher first has to have some idea of what he or she is looking for. To do this, the researcher needs to have a probe, which acts like a molecular hook that can identify and latch onto (i.e., bind to or hybridize with) the desired gene in a crowd of many other genes. A researcher who can obtain an entire strand of mRNA can eventually find the gene from which it was copied, using complementary DNA (cDNA, which is a cloned equivalent to RNA and somewhat equivalent to mRNA) as a probe to search through the great mass of genetic material and locate the desired original gene. cDNA essentially is manufactured or non-naturally occurring DNA from which all of the nonessential DNA has been removed. cDNA allows the researcher to concentrate entirely on the important portions of the gene being examined. The nonessential DNA regions are easy to recognize because when the gene is translated into protein, these regions do not wind up reflected in the protein sequence. These regions are called introns, or intervening regions. mRNA has no introns because they have been "spliced" out of the mRNA before translation. Thus, mRNA and cDNA contain only the essential information from a gene (called the exons). cDNA is the equivalent of mRNA with a complementary sequence, only the exons are present. cDNA may be produced by reverse transcription of mRNA.

The procedure of using cDNA from known mRNA as a probe to search through genetic material and locate the original gene is called molecular hybridization, and is currently one method of identifying specific genes. However, this method is less than perfect, can be extremely time consuming, and often is not even feasible because the researcher actually has to have an entire strand of cDNA from the desired gene before he or she can attempt to use this cDNA to locate and identify the particular gene. Thus, it is something of a circular problem. If the researcher cannot obtain an entire strand of mRNA or cDNA from the desired gene, then he or she must somehow design a probe from scratch to be used to identify that gene.

Oligonucleotide probes (that is, probes made up of a small number of nucleotides, such as 17 to 100), are increasingly being used to identify specific genes from genomic or cDNA libraries when the partial amino acid sequences is known. (von Heijne 1987, Ref. 15). This is a second method of determining a proper probe. Although the present implementation of this invention does not deal with cases in which the proteins have been sequenced, but rather only the DNA or mRNA, it is possible that this invention or a future implementation of it might be used with protein sequences. Such probes can also be used as primers which, when annealed to mRNAs, can be selectively extended into cDNAs. (von Heijne 1987, Ref. 15).

Because of these situations, the problem that the researcher faces is to discover or design a probe or mixture of probes that maximizes the researchers chances of successful hybridization while at the same time minimizing the amount of time and money that has to be spent on discovering or designing the probes. (von Heijne 1987, Ref. 15). Researchers in the field have determined that computer analysis can greatly expedite and simplify the search for optimal probe sequences. (von Heijne 1987, Ref. 15). However, all of the search strategies known to the present inventors are time consuming (both CPU and user time) and may be somewhat inaccurate. As stated in von Heijne, "a true optimization of the probe in terms not only of degeneracy but in terms of length, codon usage, Guanine-Cytosine (GC) avoidance, and expected signal-to-noise ratio (hybridization to target over background) is a fairly complex problem, however, and does not seem to have been automated so far." (von Heijne 1987, Ref. 15). Various search strategies known and used in the field to identify and design probes are outlined in the following sources: Lewis (1986, Ref. 9), Raupach (1984, Ref. 11), Yang et al. (1984, Ref. 16), and Martin and Castro (1984, Ref. 10).

In the simplest version of a protein-related search strategy, the search procedure is limited to finding a set of probes of given lengths with the least possible degeneracy simply by scanning the amino acid sequence and noting the number of alternative codons in the corresponding oligonucleotide as the scan moves along the chain of nucleotides. (Lewis 1986). The researcher can also include codon usage statistics (because more than one codon can translate to the same amino acid), which would attach a probability-of-occurrence value to each probe. (Raupach 1984, Ref. 11).

A more advanced algorithm would allow the researcher to specify the way in which he or she plans to synthesize the probes (for example, by adding monomers or mixtures of monomers). It would also be easy for a researcher to add a rough estimate of the disassociation (or melting) temperatures of each probe to a program such as this.

One way to solve the problem of finding local similarities between two proteins being compared that has been discussed in the relevant literature is to use list-sorting or hashing routines. (von Heijne 1987, Ref. 15). These routines are based on the construction of a list or lookup table of k-letter words or k-tuples (i.e., all possible di- or trinucleotides), and the positions where they appear in the sequences being compared. This method is employed in some of the most extensively used "fast search" programs (see examples identified in von Heijne 1987, Ref. 15).

Two general methods of designing probes are common in the field, depending upon whether the researcher is trying to design a common probe or a specific probe. Common probes attempt to find common or consensus sequences among various species and among family genes. The first step in designing such a probe is to find the genes of interest. This may be done by performing a keyword or homology search against the

GenBank (a genome database available from IntelliGenics of Mountain View, CA) or a keyword search against MEDLINE (the database currently available from the U.S. National Library of Medicine under the data access system known as Dialog of Dialog Information Service, Inc., Palo Alto, CA) or by performing a homology analysis between one of the genes of interest and whole GenBank sequences. The next step is to retrieve all of the relevant genes of interest. In the third step, multiple alignment analysis can be done using a commercially available software package such as DNASIS (from Hitachi Software of Brisbane, California), which is an autoconnect program. In this step, the computer identifies which nucleotides are common among the requested sequences:

```
A1    A G G C C T C G G T T A G T T G G C C G T T G C C G A A A AA
      : : : :   : : : : : : :   : : : :   :   : :   : :   :
A2    A G G C G T C G G T T A T T T G G G C C T T C C C A A T G TG
      : : : : : : : : : : :   :   : : :     : : : : : :   :   :
A3    A G G C G T C G G T T C T G T G G A A C T T C C C G A G G AA

      * * * *   * * * * * *       * * *       * *   * *   *

      * = common among A1, A2, and A3
```

Alternatively, after homology analyses between two sequences are carried out, data from the multiple homology analyses can be combined. The researcher then manually has to find the common or consensus region:

```
A1    A G G C C T C G G T T A G T T G G C C G T T G C C G A A A AA
      : : : : : : : : : : :   : : : :   :   : :   : :   :
A2    A G G C G T C G G T T A T T T G G G C C T T C C C A A T G TG

A2    A G G C G T C G G T T A T T T G G G C C T T C C C A A T G TG
      : : : : : : : : : : :   :   : : :     : : : : : :   :   :
A3    A G G C G T C G G T T C T G T G G A A C T T C C C G A G G AA

      * * * *   * * * * * *       * * *       * *   * *   *

      * = common among A1, A2, and A3
```

Next, the researcher would input the sequence of the common region into the program and then analyze the secondary structure (i.e., the stacking site and the hairpin structure). After this, the researcher manually would select several candidate probes (from five to ten) which contain the minimal hairpin structure and specific length according to the user's interest. A hairpin is an area in which a probe has "folded back" and one portion of the probe has hybridized with another portion of the same probe. The researcher would then perform a homology analysis between each candidate probe and all sequences in the GenBank to find all possible cross-hybridizable genes. Lastly, the researcher manually would decide which is the best candidate probe by determining which probe is highly homologous among the group of interest, but quite different from other unrelated sequences in the GenBank.

The conventional methods for designing common oligonucleotide probes using currently available computer software have at least five problems: (1) they involve time consuming multiple processes; (2) it is difficult to control a significant variable, the melting temperature Tm of the oligonucleotide probes; (3) the methods do not recognize exons and introns and differentiate (thereby making it possible to have a designed probe that is identical to unrelated mRNA sequences); (4) the methods may miss short pieces of identical sequences; and (5) it is difficult to recognize multiple pieces of identical sequences in the gene.

The second method of designing probes that is common in the field involves designing specific probes. Specific probes attempt to find unique sequences among various species and among family genes and among published sequences in the GenBank. A specific probe is a probe that hybridizes with only one particular gene, thereby identifying the presence of that gene for the researcher. The procedure involves first finding the genes of interest (by performing a keyword search against the GenBank or against MEDLINE) and then retrieving all of the relevant genes of interest. A manual homology analysis between the gene of interest and whole sequences in the GenBank can be performed to find common and unique regions.

```
A1    A G G C C T C G G T T A G T T G G C C G T T G C C G A A A AA
      : : : :   : : : : : : :   :     :       :     : :   :
B1    A G G C G T C G G T T A T T G T G G T C T C C C C A A T G TG

      - - - - - - - - - - - -     * * * * * * * * * * * * * * * **
            common                              unique
```

Next, the researcher would input the sequence of the unique region into the program and then analyze the secondary structure. After this, the researcher would manually select several candidate probes which contain the minimal hairpin structure and specific length according to the user's interest. The researcher would then perform a homology analysis between each candidate probe and all sequences in the GenBank to find all possible cross-hybridizable genes. Lastly, the researcher manually would decide which is the best candidate probe by determining which probe does not have identical sequences in unrelated sequences in the GenBank.

All of the conventional methods for designing specific oligonucleotide probes known to the inventors using currently available computer software have at least four problems: (1) they involve time consuming multiple processes; (2) it is difficult to control the melting temperature Tm of the oligonucleotide probes; (3) the methods do not allow for quantification of uniqueness; and (4) there is no guarantee that the method will design the best possible probe.

None of the methods discussed in the literature discloses a system that may be used to design both common probes and extremely specific probes, especially a method that minimizes user and CPU time and is exceptionally accurate.

Programs currently used for rapid database similarity searches use either hashing strategies or statistical strategies. The hashing strategy is now being used for the detection of relatively short regions of similarity, while the statistical strategy is now being used for the detection of weaker and longer similarity regions. The Mismatch Model of this invention can be used for very strong similarity searches with running times faster than current hashing strategies.

The basic technologies behind the Mismatch Model used in this invention are hashing and continuous seed filtration, each general technology being known in the public domain and having been previously applied separately to non-genetic applications. To the best of the inventors' knowledge, these methods, used together, have never been suggested in other studies on optimal probe selection. The inventors' methods have a program performance of tens of seconds (CPU + I/O time) with a 1000 nucleotide query and all mammalian DNA on a SPARC station, and are even faster on the more common personal computer proposed herein.

The H-Site Model of this invention likewise is unique in that it offers a multitude of information on selected probes and original and distinctive means of visualizing, analyzing and selecting among candidate probes designed with the invention. Candidate probes are analyzed using the H-Site Model for their binding specificity relative to some known set of mRNA or DNA sequences, collected in a database such as the GenBank database. The first step involves selection of candidate probes at some or all the positions along a given target. Next, a melting temperature model is selected, and an accounting is made of how many false hybridizations each candidate probe will produce and what the melting temperature of each will be. Lastly, the results are presented to the researcher along with a unique set of tools for visualizing, analyzing and selecting among the candidate probes.

This invention is both much faster and much more accurate than the methods that are currently in use. It is unique because it is the only method that can find not only the most specific and unique sequence, but also the common sequences. Further, it allows the user to perform many types of analysis on the candidate probes, in addition to comparing those probes in various ways to the target sequences and to each other.

Therefore, it is the object of this invention to provide a practical and user-friendly system that will allow a researcher to design both specific and common oligonucleotide probes, and to do this in less time and with much more accuracy than currently done. For example, the current version of the GenBank contains over ninety (90) million nucleotides. It is thought that the human genome alone consists of three billion base pairs, and scientists have so far managed to decode the base sequence of only about 500 human genes, less than one percent of the total. Currently available searching strategies are limited in how many of the GenBank's sequences can be accessed and successfully searched, and how convenient and feasible such a search would be (in terms of both computer processor and human user time). It is also an object of this invention to allow the user to be able to run the program on more readily available and far less expensive computer hardware (i.e., a PC rather than a mainframe). This invention will remove those limits and allow genetic research to take a giant leap forward.

These and other advantages and objects of this invention will become apparent from the following detailed descriptions, drawings, and appended claims.

BRIEF DESCRIPTION OF THE INVENTION

There is disclosed herein a system which allows the user to calculate and design extremely accurate oligonucleotide probes for DNA and mRNA hybridization procedures. The invention runs under Microsoft® Windows on IBM® compatible personal computers (PC's). Its key features design oligonucleotide probes based on the GenBank database of DNA and mRNA sequences and examine probes for specificity or commonality with respect to a user-selected experimental preparation of gene sequences. Hybridization strength between a probe and a subsequence of DNA or mRNA can be estimated through a hybridization strength model. Quantitatively, hybridization strength is given as the melting temperature Tm. Currently, two hybridization strength models are supported by this invention: 1) the Mismatch Model and 2) the H-Site Model. The user is allowed to select from the following calculations for each probe, results of which are available for display and analysis: 1) Sequence, Melting Temperature (Tm) and Hairpin characteristics; 2) Hybridization with other species within the preparation mixture; and (3) Location and Tm for the strongest hybridizations. The results of the invention's calculations are then displayed on the Mitsuhashi Probe Selection Diagram (MPSD), which is a graphic display of all of the hybridizations of probes for the target mRNA with all sequences in the preparation.

The Main Dialog Window of the present implementation of this invention controls all user-definable settings. The user is offered a number of options at this window. The File option allows the user to print, print in color, save selected probes, and exit the program. The Preparation option allows the user to open and create preparation (PRP) files. The Models option allows the user to chose between the two hybridization models currently supported by the invention: 1) the H-Site Model and 2) the Mismatch Model. If the user selects the H-Site Model option, the user normally sets the following model parameters: 1) the melting temperature Tm for which probes are being designed (i.e.,the melting temperature that corresponds to a particular experiment or condition the user desires to simulate); and 2) the nucleation threshold, which is the number of base pairs constituting a nucleation site. If the user selects the Mismatch Model option, the user normally sets the following model parameters: 1) probe length, which is the number of bases in probes to be considered; and 2) mismatch N, which is the maximum number of mismatches constituting a hybridization.

The Mismatch Model program is used to design DNA and mRNA probes, utilizing sequence database information from sources such as GenBank and other databases with similar file formats. In the Mismatch Model, hybridization strength is related only to the number of base pair mismatches between a probe and its binding site. Generally, the more mismatches a user allows, the more probes will be found. The Mismatch Model does not take into account the Guanine-Cytosine (GC) content of candidate probes, as does the H-Site Model, discussed below, so there is no reflection or indication of the probe's binding strength. The basic technologies employed by this model are hashing and continuous seed filtration. Hashing involves the application of an algorithm or process to the records in a set of data to obtain a symmetric grouping of the records. When using an indexed set of data, hashing is the process of transforming a record key to an index value for storing and retrieving a record. Rosenberg (1984, Ref. 12)). The concept of continuous seed filtration is discussed in detail below.

The essence of the Mismatch Model is a fast process for doing exact and inexact matching between DNA and mRNA sequences to support the Mitsuhashi Probe Selection Diagram (MPSD) and other types of analysis discussed above. The process used by the Mismatch Model is the Waterman-Pevzner Algorithm (the WPALG, which is named for two of the inventors), which is a computer-based probe selection process. Essentially, this is a combination of new and improved pattern matching processes. See Hume and Sunday (1991, Ref. 4), Landau et al (1986-1990, Refs. 6, 7, 8), Grossi and Luccio (1989, Ref. 3), and Ukkonen (1982, Ref. 14).

There are three principal programs that make up the Mismatch Model in this implementation of the invention. The first is designated by the inventors as "k_diff." WPALG is used in k_diff to find all locations of matches of length greater than or equal to one (1) (length is user-specified) with less than or equal to k number of mismatches (k is also user-specified) between the two sequences. If a candidate oligonucleotide probe fails to match that well, it is considered unique. k_diff uses hashing and continuous seed filtration, and looks for homologs in GenBank and other databases with similar file formats. The technique of continuous seed filtration allows for much more efficient searching than previously implemented techniques. A seed is defined in this invention to be a subsequence of length equal to the longest exact match in the worst case scenario. For example, suppose the user selects a probe length (l) of 18, with 2 or fewer mismatches (k). If a match exists with 2 mismatches, then there must be a perfectly matching subsequence of length equal to 6. Once the seed length has been determined, the Mismatch Model looks at all substrings of that seed length (in this example, that seed length would be 6), finds the perfectly matched base pair subsequence of length equals 6, and then looks to see if this subsequence extends to a sequence of length equal to the user selected probe length (i.e., 20 in this example). If so, a candidate probe has been found that meets the user's criteria.

Where the seed size is large, the program allocates a relatively large amount of memory for the hash table. This invention has an option that allows memory allocation for GenBank entries just once at the beginning of the program, instead of reallocating memory for each GenBank entry. This reduces input time for GenBank entries by as much as a factor of two (2), but the user needs to know the maximum GenBank entry size in advance to do this.

A probe is defined to hybridize if it has k or fewer mismatches in comparison with a target sequence from the database or file searched. Otherwise, it is non-hybridizing. The hit extension time for all appropriate parameters of the Mismatch Model has been found by experimentation to be less than thirty-five (35) seconds, except in one case where the minimum probe length (l) was set to 24 and the maximum number of mismatches (k) was set to four (4), which is a situation that is never used in real gene localization experiments because the hybridization conditions are too weak.

In this invention, the second hybridization strength model is termed the H-Site Model. One aspect of the H-Site Model uses a generalization of an experimental formula in general usage. The basic formula on which this aspect of the model is built is as follows:

$$Tm = 81.5 - 16.6(\log[Na]) - .63\ \%(\text{formamide}) + .41\ (\%(G + C)) - 600\ / \ N$$

In this formula, log[Na] is the sodium concentration, %(G + C) is the fraction of matched base pairs which are G-C complementary, and N is the probe length. In other words, this formula is an expression of the fact that melting temperature Tm is a function of both probe length and percent of Guanine-Cytosine (GC) content. This basic formula has been modified in this invention to account for the presence of mismatches. Each percent of mismatch reduces the melting temperature Tm by an average of 1.25 degrees (2 degrees C for an Adenine-Thymine mismatch, and 4 degrees C for a Guanine-Cytosine mismatch). This formula is, however, an approximation. The actual melting temperature might differ significantly from this approximation, especially for short probes or for probes with a relatively large number of mismatches.

Hybridization strength in the H-Site Model is related to each of the following factors: 1) "binding region"; 2) type of mismatch (GC or AT substitution); 3) length of the probe; 4) GC content of the binding region (since GC pairs have a stronger bond than AT pairs, thus requiring a higher melting temperature); and 5) existence of a "nucleation site" (an exactly matching subsequence). The type of mismatch and the GC content of the binding region each contribute to a candidate probe's binding strength, which can be compared to other candidate probes' binding strengths to enable the user to select the optimal probe.

The fundamental assumption of the H-Site Model is that binding strength is determined by a paired subsequence of the probe-species combination, called the binding region. If the binding region contains more GC pairs than AT pairs, the binding strength will be higher since the G and C bases (connected with three bonds) form a tighter bond than the A and T bases (connected with two bonds). Thus, G and C bases, and probes that are GC rich, require a higher melting temperature Tm and subsequently form a stronger bond. In the H-Site Model, and one of its unique features, the program designs optimal probes, ideally ones that do not have any mismatches, but if there are mismatches the H-Site Model takes these into account. With this model, a candidate probe can afford to have more mismatches involving the AT bases if there are more GC bases than AT bases in the probe. This is because this model looks primarily at regions of the candidate probe and target sequence that match and does not "penalize" the probe for areas that do not match. If the mismatches are located at either or both of the ends of the binding region, this has little effect. It is much more deleterious to have mismatches in the middle of the binding region, as this will significantly lower the binding strength of the probe.

The formula cited above for Tm applies within the binding region. The length of the probe is used to calculate percentages, but all other parameters of the formula are applied to the binding region only. The H-Site Model further assumes the existence of a nucleation site, which is a region of exact match. The length of this nucleation site may be set by the user. Typically, a value of 8 to 10 base pairs is used. To complete the H-Site Model, the binding region is chosen so as to maximize the melting temperature Tm among all regions containing a nucleation site, assuming one exists (otherwise, Tm=0).

The H-Site Model is more complex than the Mismatch Model discussed above in that hybridization strength is modeled as a sum of signed contributions, with matches generally providing positive binding energy and mismatches generally providing negative binding energy. The exact coefficients to be used depend only on the matched or mismatched pair. These coefficients may be specified by the user, although in the current version of this invention these coefficients are not explicitly user-selectable, but rather are selected to best fit the hybridization strength formulas developed by Itakura et al (1984, Ref. 5), Bolton and McCarthy (1962, Ref. 2), Benner et al (1973, Ref. 1), and Southern (1975, Ref. 13).

A unique aspect of the H-Site Model is that hybridization strength is defined to be determined by whatever the optimal binding region between the candidate probe and binding locus. This binding region is called the hybridization site, or h-site, and is selected so as to maximize overall hybridization strength, so that mismatches outside the binding region do not detract from the estimated hybridization strength. Several other unique features of the H-Site Model include the fact that it is more oriented toward RNA and especially cDNA sequences than DNA sequences, and the fact that the user has control over preparation and environmental variables. The first feature allows the user to concentrate on "meaningful" sequences, rather than having to sort through all of a DNA sequence (including the introns). The second feature allows the user to more accurately simulate laboratory conditions and more closely correspond with any experiments he or she is conducting. Further, this implementation of the invention does some preliminary preprocessing of the GenBank database to sort out and select the cDNA sequences. This is done by locating a keyword (in this case CDS) in each GenBank record, thereby eliminating any sequences containing introns.

The Mitsuhashi Probe Selection Diagram (MPSD),. FIG. 4, is the third key feature of this invention, as it is a unique way of visualizing the results of the probe designing performed by the Mismatch and H-Site Models. It is a graphic display of all of the hybridizations of candidate oligonucleotide probes for the target mRNA with all sequences in the preparation. Given a gene sequence database and a target mRNA sequence, the MPSD graphically displays all of the candidate probes and their hybridization strengths with all sequences from the database. In the present implementation, each melting temperature Tm is displayed as a different color, from red (highest Tm) to blue (lowest Tm). The MPSD allows the user to see visually the number of false hybridizations at various temperatures for all candidate probes, and the sources of these false hybridizations (with a loci and sequence comparison). A locus may be a specific site or place, or, in the genetic sense, a locus is any of the homologous parts of a pair of chromosomes that may be occupied by allelic genes.

BRIEF DESCRIPTION OF THE DRAWING

This invention may be more clearly understood from the following detailed description and by reference to the drawing in which:

FIG. 1 is a simplified block diagram of a computer system illustrating the overall design of this invention;

FIG. 2 is a display screen representation of the main dialog window of this invention;

FIG. 3 is a flow chart of the overall invention illustrating the program, and the invention's sequence and structure;

FIG. 4 is a display screen representation of the Mitsuhashi probe selection diagram;

FIG. 5 is a display screen representation of the probeinfo and matchinfo window;

FIG. 6 is a display screen representation of the probesedit window;

FIG. 6a is a printout of the probesedit output file;

FIG. 7 is a flow chart of the overall k_diff program of the Mismatch Model of this invention, including its sequence and structure;

FIG. 8 is a flow chart of the k_diff module of this invention;

FIG. 9 is a flow chart of the hashing module of this invention;

FIG. 10 is a flow chart of the tran module of this invention;

FIG. 11 is a flow chart of the let_dig module of this invention;

FIG. 12 is a flow chart of the update module of this invention;

FIG. 13 is a flow chart of the assembly module of this invention;

FIG. 14 is a flow chart of the seqload module of this invention;

FIG. 15 is a flow chart of the read1 module of this invention;

FIG. 16 is a flow chart of the dig_let module of this invention;

FIG. 17 is a flow chart of the q_colour module of this invention;

FIG. 18 is a flow chart of the hit_ext module of this invention;

FIG. 19 is a flow chart of the colour module of this invention;

FIG. 20 is a printout of a sample file containing the output of the Mismatch Model program of this invention;

FIG. 21 is a flow chart of the H-Site Model, stage I, covering the creation of a preprocessed preparation file of this invention;

FIG. 22 is a flow chart of the H-Site Model, stage II, covering the preparation of the target sequence(s);

FIG. 23 is a flow chart of the H-Site Model, stage III, covering the calculation of MPSD data;

FIG. 24a is a printout of a sample file containing output of the Mismatch Model program;

FIG. 24b is a printout of a sample file containing output of the H-Site Model program;

FIG. 25 is a flow chart of the processing used to create the Mitsuhashi probe selection diagram (MPSD);

FIG. 26 is a flow chart of processing used to create the matchinfo window;

FIG. 27 is a printout of a sample target species file;

FIG. 28 is a printout of a sample preparation file.

DETAILED DESCRIPTION OF THE INVENTION

This invention is employed in the form best seen in FIG. 1. There, the combination of this invention consists of an IBM® compatible personal computer (PC), running software specific to this invention, and having access to a distributed database with the file formats found in the GenBank database and other related databases.

The preferred computer hardware capable of operating this invention involves of a system with at least the following specifications (FIG. 1): 1) an IBM® compatible PC, generally designated 1A, 1B, and 1C, with an 80486 coprocessor, running at 33 Mhz or faster; 2) 8 or more MB of RAM, 1A; 3) a hard disk 1B with at least 200 MB of storage space, but preferably 1 GB; 4) a VGA color monitor 1C with graphics capabilities of a size sufficient to display the invention's output in readable format, preferably with a resolution of 1024 x 768; and 5) a 580 MB CD ROM drive 5 (1B of FIG. 1 generally refers to the internal storage systems included in this PC, clockwise from upper right, two floppy drives, and a hard disk). Because the software of this invention preferably has a Microsoft® Windows™ interface, the user will also need a mouse 2, or some other type of pointing device.

The preferred embodiment of this invention would also include a laser printer 3 and/or a color plotter 4. The invention may also require a modem (which can be internal or external) if the user does not have access to the CD ROM versions of the GenBank database 8 (containing a variable number of gene sequences 6). If a modem is used, information and instructions are transmitted via telephone lines to and from the GenBank database 8. If a CD ROM drive 5 is used, the GenBank database (or specific portions of it) is stored on a number of CDs.

The computer system should have at least the Microsoft® DOS v. 5.0 operating system running Microsoft® Windows™ v. 3.1. All of the programs in the preferred embodiment of the invention are written in the Borland® C++ (made by Borland International, Inc., of Scotts Valley, CA) computer language. It must be recognized that subsequently developed computers, storage systems, and languages may be adapted to utilize this invention and vice versa.

This invention is designed to enable the user to access DNA, mRNA and cDNA sequences stored either in the GenBank or in databases with similar file formats. GenBank is a distributed flat file database made up of records, each record containing a variable number of fields in ASCII file format. The stored database itself is distributed, and there is no one database management system (DBMS) common to even a majority of its users. One general format, called the line type format, is used both for the distributed database and for all of GenBank's internal record keeping. All data and system files and indexes for GenBank are kept in text files in this line type format.

The primary GenBank database is currently distributed in a multitude of files or divisions, each of which represents the genome of a particular species (or at least as much of it as is currently known and sequenced and publicly available). The GenBank provides a collection of nucleotide sequences as well as relevant bibliographic and biological annotation. Release 72.0 (6/92) of the GenBank CD distribution contains over 71,000 loci with a total of over ninety-two (92) million nucleotides. GenBank is distributed by IntelliGenetics, of Mountain View, CA, in cooperation with the National Center for Biotechnology Information, National Library of Medecinge, in Bethesda, MD.

1. Overall Description of the Invention

a. **General Theory**

The intent of this invention is to provide one or more fast processes for performing exact and inexact matching between DNA sequences to support the Mitsuhashi Probe Selection Diagram (MPSD), discussed below, and other analysis with interactive graphical analysis tools. Hybridization strength between a candidate oligonucleotide probe and a subsequence of DNA, mRNA or cDNA can be estimated through a hybridization strength model. Quantitatively, hybridization strength is given as the melting temperature Tm. Currently, two hybridization strength models are supported by the invention: 1) the Mismatch Model and 2) the H-Site Model.

b. **Inputs**

i. Main Dialog Window

The Main Dialog Window, FIG. 2, controls all user-definable settings. This window has a menu bar offering five options: 1) File 10; 2) Preparation 20; 3) Models 30; 4) Experiment 40; and 5) Help 50. The File 10 option allows the user to print, print in color, save selected probes, and exit the program. The Preparation 30 option allows the user to open and create preparation (PRP) files.

The Models 20 option allows the user to chose between the two hybridization models currently supported by the invention: 1) the H-Site Model 21 and 2) the Mismatch Model 25. If the user selects the H-Site Model 21 option, the left hand menu of FIG. 2C is displayed and the user sets the following model parameters: 1) the melting temperature Tm 22 for which probes are being designed (i.e., the melting temperature that corresponds to a particular experiment or condition the user desires to simulate); and 2) the nucleation threshold 23, which is the number of base pairs constituting a nucleation site. If the user selects the Mismatch Model 25 option, the right hand menu of FIG. 2C is displayed and the user sets the following model parameters: 1) probe length 26, which is the number of base pairs in probes to be considered; and 2) mismatch N 27, which is the maximum number of mismatches constituting a hybridization. Computation of the user's request will take longer with the H-Site Model if the threshold 23 setting is decreased and with the Mismatch Model if the number of mismatches K 27 is increased.

In addition, for both Model options the user chooses the target species 11 DNA or mRNA for which probes are being designed and the preparation 12, a file of all sequences with which hybridizations are to be calculated. A sample of a target species file is shown in FIG. 27 (humbjunx.cds), while a sample of a preparation file is shown in FIG. 28 (junmix.seq). Each of these inputs is represented by a file name and extension in general DOS format. In the target species and preparation fields, the file format follows the GenBank format, and each of the fields includes a default file extension. Pressing the "OK" button 41 of FIG. 2C will cause the processing to begin, and pressing the "Cancel" button 43 will cause it to stop.

The Experiment 40 option and the Help 50 option are expansion options not yet available in the current implementation of the invention.

c. **Processing**

FIG. 3 is a flow chart of the overall program, illustrating its sequence and structure. Generally, the main or "control" program of the invention basically performs overall maintenance and control functions. This program, as illustrated in FIG. 3, accomplishes the general housekeeping functions 51, such as defining global variables. The user-friendly interface 53, carries out the user-input procedures 55, the file 57 or database 59 access procedures, calling of the model program 62 or 63 selected by the user, and the user-selected report 65 or display 67, 69, 71 and 73 features. Each of these features is discussed in more detail in later sections, with the exception of the input procedures, which involves capturing the user's set-up and control inputs.

d. **Outputs**

i. <u>The Mitsuhashi Probe Selection Diagram Window</u>

The Mitsuhashi Probe Selection Diagram (MPSD), FIG. 4, is a key feature of the invention as it is a unique way of visualizing the results of the program's calculations. It is a graphic display of all of the hybridizations of probes for the target mRNA with all sequences in the preparation. In other words, given a sequence database and a target mRNA, the MPSD graphically displays all of the candidate probes and their hybridization strengths with all sequences from the sequence database. The MPSD allows the user to see visually the number of false hybridizations at various temperatures for all candidate probes, and the sources of these false hybridizations (with a loci and sequence comparison).

For each melting temperature Tm of interest, a graphical representation of the number of hybridizations for each probe is displayed. In the preferred embodiment, this representation is color coded. In this implementation of the invention, the color red 123 identifies the highest melting temperature Tm and the color blue 124 identifies the lowest melting temperature Tm. Each mismatch results in a reduction in Tm. Tm is also a function of probe length and percent content of GC bases. Within the window, the cursor 125 shape is changed from a vertical line bisecting the screen to a small rectangle when the user selects a particular probe. The current probe is defined to be that probe under the cursor position (whether it be a line or a rectangle) in the MPSD window. More detailed information about the current probe is given in the ProbeInfo and MatchInfo windows, discussed below. Clicking the mouse 2 once at the cursor 125 selects the current probe. Clicking the mouse 2 a second time deselects the current probe. Moving the cursor across the screen causes the display to change to reflect the candidate probe under the current cursor position.

The x-axis 110 of the MPSD, FIG. 4, shows the candidate probes' starting positions along the given mRNA sequence. The user may "slide" the display to the left or right in order to display other probe starting positions. The y-axis 115 of the MPSD displays the probe specificity, which is calculated by the program.

The menu options 116, 117, 118, 119, and 120 available to the user while in the MPSD, FIG. 4, are displayed along a menu bar at the top of the screen. The user can click the mouse 2 on the preferred option to briefly display the option choices, or can click and hold the mouse button on the option to allow an option to be selected. The user may also type a combination of keystrokes in order to display an option in accordance with well-known computer desk top interface operations. This combination usually involves holding down the ALT key while pressing the key representing the first letter of the desired option (i.e, F, P, M, E or H).

The File option 116 allows the user to specify input files and databases. The Preparation option 117 allows the user to create a preparation file summarizing the sequence database. The Models option 118 allows the user to specify the hybridization model (i.e., H-Site or Mismatch) and its parameters. The Experiment option 119 and the Help option 120 are not available in the current implementation of this invention. These options are part of the original Main Dialog Window, FIG. 2.

Areas on the graphical display of the MPSD, FIG. 4, where the hybridizations for the optimal probes are displayed are lowest and most similar, such as shown at 121, indicate that the particular sequence displayed is common to all sequences. Areas on the graphical display of the MPSD where the hybridizations for the optimal probes are displayed are highest and most dissimilar, such as shown at 122, indicate that the particular sequence displayed is extremely specific to that particular gene fragment. The high points on the MPSD show many loci in the database, to which the candidate probe will hybridize (i.e., many false hybridizations). The low points show few hybridizations, at least relative to the given database. In other words, the sequence shown at 121 would reflect a probe common to all of the gene fragments tested, such that this probe could be used to detect each of these genes. The sequence shown at 122 would reflect a probe specific to the particular gene fragment, such that this probe could be used to detect this particular gene and no others.

ii. The ProbeInfo and MatchInfo Window

The combined ProbeInfo and MatchInfo Window, FIG. 5, displays detailed information about the current candidate probe. The upper portion of the window is the ProbeInfo window, and the lower portion is the MatchInfo window. The ProbeInfo window portion displays the following types of information: the target locus (i.e., the mRNA, cDNA, or DNA from which the user is looking for probes) is displayed at 131, while the preparation used for hybridizations is displayed at 132. In the example shown in FIG. 5, the target locus 131 is the file named HUMBJUNX.CDS, which is shown as being located on drive F in the subdirectory MILAN. The preparation 132 is shown as being the file designated JUNMIX.PRP, which is also shown as being located on drive F in the subdirectory MILAN. The JUNMIX.PRP preparation in this example is a mixture of human and mouse jun loci.

The current and optimal probe's starting position is shown at 135. The current candidate oligonucleotide probe is defined at 136, and is listed at 137 as having a length of 21 bases. The melting temperature for the probe 136 as hybridized with the targets is shown in column 140. The melting temperature for the optimal probe is given as 61.7 degrees C at 138. The ProbeInfo Window FIG. 5 also displays hairpin characteristics of the probe at 139. In the example shown, the ProbeInfo Window shows that there are four (4) base pairs involved in the worst hairpin, and that the worst hairpin has a length of one (1) (see FIG. 5, at 139).

The MatchInfo Window portion displays a list of hybridizations between the current probe and species within the preparation file, including hybridization loci and hybridization temperatures. The hybridizations are listed in descending order by melting temperature. The display shows the locus with which the hybridization occurs, the position within the locus, and the hybridization sequence.

In the MatchInfo window portion, the candidate probe 136 is shown at 150 as hybridizing completely with a high binding strength. This is because the target DNA is itself represented in the database in this case, so the candidate probe is seen at 150 to hybridize with itself (a perfect hybridization). The locus of each hybridization from the preparation 132 are displayed in column 141, while the starting position of each hybridization is given in column 142. The calculated hybridizations are shown at 145.

iii. The ProbesEdit Window

The ProbesEdit Window, FIG. 6, is a text editing window provided for convenient editing and annotation of the invention's text file output. It is also used to accumulate probes selected from the MPSD, FIG. 4, by mouse 2 clicks. Standard text editing capabilities are available within the ProbesEdit Window. The user may accumulate selected probes in this window (see 155 for an example) and then save them to a file (which will bear the name of the preparation sequence with the file extension of "prb" 156, or may be another file name selected by the user). A sample of this file is shown in FIG. 6A.

iv. Miscellaneous Output

The present embodiment of this invention also creates two output files, currently named "test.out" and "test1.out", depending upon which model the user has selected. The first file, "test.out", is created with both the Mismatch Model and the H-Site Model. This file is a textual representation of the Mitsuhashi Probe Selection Diagram (MPSD). It breaks the probe sequence down by position, length, delta Tm, screensN, and the actual probe sequence (i.e., nucleotides). An example of this file created by the Mismatch Model is shown in FIG. 20, and example created by the H-Site Model is shown in FIG. 24A. The second file, "test1.out", is created only by the H-Site Model. This file is a textual representation of the ProbeInfo and MatchInfo window that captures all hybridizations, along with their locus, starting position, melting temperature, and possible other hybridizations. A partial example of this file is shown in FIG. 24B (10 pages out of a total of 190 pages created by the H-Site Model).

2. Description of the Mismatch Model Program

a. Overview

In this invention, one of the hybridization strength models is termed the Mismatch Model (see FIG. 2 for selection of this model). The basic operation of this model involves the techniques of hashing and continuous seed filtration, as defined earlier and described in more detail below. The essence of the Mismatch Model is a fast process for doing exact and inexact matching between DNA and mRNA sequences to support the Mitsuhashi Probe Selection Diagram (MPSD). There are a number of modules in the present implementation of the Mismatch Model contained in this invention, the most significant of which are shown in the flow chart in FIG. 7 and in more detail in FIGS. 8 through 18. The main k_diff module shown in the flow chart in FIG. 8 is a structured program that provides overall control of the Mismatch Model, calling various submodules that perform different functions.

b. Inputs

The user-selected input variables for this model are minimum probe length 26 (which is generally from 18 to 30) and maximum number of mismatches 27 (which generally is from 1 to 5). These inputs are entered by the user in the Main Dialog Window, FIG. 2C.

c. Processing

i. k_diff Program

Some terms of art need to be defined before the processing performed by this module can be explained. A hash table basically is an array or table of data. A linked list is a classical data structure which is a chain of linked entries and involves pointers to other entry structures. Entries in a linked list do not have to be stored sequentially in memory, as is the case with elements contained in an array. Usually there is a pointer to the list associated with the list, which is often initially set to point to the start of the list. A pointer to a list is useful for sequencing through the entries in the list. A null pointer (i.e., a pointer with a value of zero) is used to mark the end of the list.

As the flow charts in FIGS. 7 and 8 illustrate, the general process steps and implemented functions of this model can be outlined as follows:

```
Step 1: First, create a hash table and linked list from the query (FIG. 7, hashing module 222).
Step 2: Next, while there are still GenBank entries available for searching (FIG. 7, assembly module 230):
    Step 2a: Read the current GenBank entry (record) sequence of user-specified length (FIG. 7, seqload module 232), or read the current sequence (record) from the file selected by the user (FIG. 7, read1 module 234).
    Step 2b: For the current sequence for each position of the sequence from the first position (or nucleotide) to the last position (or nucleotide) (incrementing the position number once each iteration of the loop) (FIG. 7, q_colour module 242),
        Step 2c: set the variable dna_hash equal to the hash of the current position of the current sequence (FIG. 7, q_colour module 242).
        Step 2d: While not at the end of the linked list for dna_hash (FIG. 7, q_colour module 242),
            Step 2e: set the query_pos equal to the current position of dna_hash in the linked list (FIG. 7, q_colour module 242) and
            Step 2f: Extend the hit with the coordinates (query_pos, dna_pos) (FIG. 7, hit_ext module 244),
            Step 2g: If there exists a k_mismatch in the current extended hit (FIG. 7, colour module 246), then
                Step 2h: print the current hit (FIG. 7, q_colour module 242), and repeat from Step 2.
```

As this illustrates, there are three (3) basic looping or iteration processes with functions being performed based on variables such as whether the GenBank section end has been reached (the first "WHILE" loop, Step 2), whether the end of the current DNA entry has been reached (the "FOR" loop, Step 2b), and whether the end of the dna_hash linked list has been reached (the second "WHILE" loop, Step 2d). A "hit" will only be printed if there are k_mismatches in the current extended hit.

FIGS. 8 through 18 illustrate the functions of each of the modules of the present embodiment of this invention, all of which were generalized and summarized in the description above. FIG. 8, which outlines the main "k_diff" module, shows that this module is primarily a program organization and direction module, in addition to performing routine "housekeeping" functions, such as defining the variables and hash tables 251, checking if the user-selected gene sequence file is open 252, extracting needed identification information from the GenBank 253, and ensuring valid user input 254. This module also performs a one-time allocation of memory for the gene sequences, and allocates memory for hit information, hashing, hybridization and frequency length profiles and output displays, 255 & 256. The "k_diff" module also initializes or "zeros out" the hashing table, the linked hashing list and the various other variables 257 in preparation for the hashing function. In addition, this module forms the hash tables 258 and extracts a sequence and finds the sequence length 259.

One of the most important functions performed by the "k_diff" module is to define the seed (or kernel or k_tuple) size. This is done by setting the variable k_tuple equal to (min_probe_length - max_mismatch_#)/(max_mismatch+# + 1) FIG. 8 at 265. Next, if the remainder of the aforementioned process is not equal to zero 266, then the value of the variable k_tuple is incremented by one 267. The resulting value is the size of the seed. The module then reads the query 268 and copies the LOCUS name 269 for identification purposes (a definition of the term locus is given earlier in the specification).

The "k_diff" module FIG. 8 also calls the "assembly" module 260, writes the results to a file 261a, plots the results 261b (discussed below), calculates the hairpin characteristics 262 (i.e., the number of base pairs and the length of the worst hairpin) and the melting temperature (Tm) for each candidate probe 263, and saves the results to a file 264.

The screen graphs are plotted 261b by converting the result values to pixels, filing a pixel array and performing a binary search into the pixel array. Next, given the number of pixels per probe position and which function is of interest to the user (i.e., the three mismatch match numbers), the program interpolates the values at the value of (pixelsPerPositionN-1) and computes the array of pixel values for drawing the graph. These values are then plotted on the MPSD.

The "hashing" module, FIG. 9, performs hashing of the query. In other words, 'it creates the hash table and linked list of query positions with the same hash. The variable has_table[i] equals the position of the first occurrence of hash i in the query. If i does not appear in the query, hash_table[i] is set to zero.

The "tran" module, FIG. 10, is called by the "hashing" module 271, and performs the hashing of the sequence of k_tuple (kernel or seed) size. If the k_tuple exists (i.e., its length is greater than zero), the variable uns is set equal to uns*ALF+p 291. The variable p represents the digit returned by the "let_dig" module FIG. 11 that represents the nucleotide being examined. ALF is a constant that is set by the program in this implementation to equal four. The query pointer is then incremented, while the size of k_tuple (the seed) is decremented 292. This process is repeated until the sequence of k_tuple has been entirely hashed. Then the "tran" module returns the variable current_hash 293 to the "hashing" module FIG. 9.

The "let_dig" module, FIG. 11, is called by the "tran" module 291, and transforms the nucleotides represented as the characters "A","T","U","G" and "C" in the GenBank and the user's query into numeric digits for easier processing by the program. This module transforms "a" and "A" into "0"301, "t","T","u" and "U" into "1"302, "g" and "G" into "2"303, and "c" and "C" into "3"305. If the character to be transformed does not match any one of those listed above, the module returns "-1" 305. The "hashing" module, FIG. 9, then calls the "update" module 272, FIG. 12, which updates the hash with a sliding window (i.e., it forms a new hash after shifting the old hash by "l"). The remainder of old_hash divided by power_1 is calculated 311 (a modulus operation), the remainder is multiplied by ALF 312 (i.e., four), and then the digit representing the nucleotide is added to the result 313. The "update" module then returns the result 314 to the "hashing" module FIG. 9.

If the current hash has already occurred in the query, the program searches for the end of the linked list for the current hash 273 and marks the end of the linked list for the current hash 274. If the current hash has not already occurred in the query, the program puts the hash into the hash table 275. The resulting hash table and linked list are then returned to the "k_diff" module, FIG. 8 at 258.

The "assembly" module, FIG. 13, extracts sequences from the GenBank and performs hit locating and extending functions. This module is called by the "k_diff" module FIG. 8 at 260 if the user has chosen to use the database to locate matches. The output from the "assembly" module (FIG. 13) tells the user that the section of the database searched contains E number of entries 321 of S summary length 322 with H number of hits 323. Further, the program tells the user that the number of considered l-tuples equals T 324. The entry head line is also printed 326.

The "seqload" module, FIG. 14, is called by the "k_diff" module FIG. 8 at 259 once the query hash table and linked list have been formed by the "hashing" module FIG. 9. The "seqload" module FIG. 14 checks to see if the end of the GenBank file has been reached 327, and, if not, searches until a record is found with LOCUS in the head-line 328. Next, the LOCUS name is extracted 329 for identification purposes, and the program searches for the ORIGIN field in the record 330.

The program then extracts the current sequence 331 from the GenBank and performs two passes on each sequence. The first is to determine the sequence length 332 and allocate memory for each sequence 333, and the second pass is to read the sequence into the allocated memory 334. Since the sequences being extracted can contain either DNA nucleotides or protein nucleotides, the "seqload" module can recognize the characters "A","T","U","G",and "C". The bases "A","T","G"and "C"are used in DNA sequences, while the bases "A","U","G" and "C"are used in RNA and mRNA sequences. The extracted sequence is then positioned according to the type of nucleotides contained in the sequence 335, and the process is repeated. Once the end of the sequence has been reached, the "seqload" module returns the sequence length 336 to the "k_diff"module FIG. 8.

If the user has chosen to use one or more files to locate matches, rather than the database, the "read1" module, FIG. 15, rather than the "seqload" module FIG. 14, is called by the "k_diff"module FIG. 8. The "read1" module, FIG. 15, reads the sequence from the user specified query file 341 and allocates memory 342. This module also determines the query length 343, extracts sequence identification information 344, determines the sequence length 345, transforms each nucleotide into a digit 346 by calling the "let_dig" module FIG. 11, creates the query hash table 347 by calling the "dig_let: module FIG. 16, and closes the file 348 once everything has been read in.

First, the "read1" module FIG. 15 allocates space for the query 342. To do this, the "ckalloc" module, FIG. 15 at 342, is called. This module allocates space and checks whether this allocation is successful (i.e., is there enough memory or has the program run out of memory). After allocating space, the "read1" module FIG. 15 opens the user-specified file 349 (the "ckopen" module, FIG. 15 at 349, is called to ensure that the query file can be successfully opened 349), determines the query length 343, locates a record with LOCUS in the head-line and extracts the LOCUS name 344 for identification purposes, locates the ORIGIN field in the record and then reads the query sequence from the file 341. Next, the sequence length is determined 345, memory is allocated for the sequence 342, and the sequence is read into the query file 350. If the string has previously been found, processing is returned to 344. If not, then each character in the query file is read into memory 350.

The characters are transformed into digits 346 using the "let_dig" module, FIG. 11, until a valid digit has been found, and then the hash table containing the query is set up 347 using the module "dig_let", FIG. 16, which transforms the digits into nucleotides represented by the characters "A"371, "T"371, "G"373, "C"374, and "X"375 as a default. If the end of the file has not been reached, processing is returned to 344. If it has, the file is closed 348 and the query is then returned to the "read1" module FIG. 15 at 347.

The "q_colour" module, FIG. 17 (FIG. 13 at 325), is called by the "assembly" module FIG. 13 after the current sequence has been extracted from the GenBank. The "q_colour" module FIG. 17 performs the heart of the Mismatch Model process in that it performs the comparison between the query and the database or file sequences. If the module finds that there exists a long (i.e., greater than the min_hit_length) extended hit, it returns a "1"to the "assembly" module FIG. 14. Otherwise, the "q_colour" module, FIG. 17, returns a "0".

In the "q_colour" module, FIG. 17, all DNA positions are analyzed in the following manner. First, the entire DNA sequence is analyzed 391 to see whether each position is equal to zero 392 (i.e., whether it is empty or the sequence is finished). If it is not equal to zero 393, the "q_colour" module FIG. 20 calls the "tran" module, FIG. 10 described above, which performs the hashing of k_tuples. The "tran" module FIG. 10 calls other modules which transform the nucleotides represented by characters into digits for easier processing by the program and then updates the hash with a sliding window. If the position is equal to zero, the current_hash position is set to new_has after one shift of old_hash 390 by calling the "update" module FIG. 12.

If the nucleotide at the current_hash position is equal to zero, processing is returned to 391. If not, the query position is set equal to (nucleotide at current hash position - 1). Next, the "q_colour" module FIG. 17 looks for the current_hash in the hash table 394. If the current k_tuple does not match the query 395, then the next k_tuple is considered 395, and processing is returned to 391. If the current k_tuple does match the query, then the program checks the hit's (i.e., the match's) vicinity 396 by calling the "hit_ext" module, FIG. 18 to determine if the hit is weak. The inventors have found that if the code for the module "hit_ext" is included within the module "q_colour", rather than being a separate module utilizing the parameter transfer machinery, 25% of CPU time can be saved.

The "hit_ext" module FIG. 18 determines the current query position in the hit's vicinity 421, determines the current DNA position in the hit's vicinity 422, and creates the list of mismatch positions (i.e., the mismatch_location_ahead 423, the mismatch_location_behind 423 and the kernel match location). If the hit is weak 424, the "hit_ext" module FIG. 18 returns "0"to the "q_colour" module FIG. 17. If the hit has a chance to contain 425, the module returns "1"to the "q_colour" module FIG. 17. A hit has a chance to contain, and is therefore not considered weak, if the mismatch_location_ahead - the mismatch_location_behind is greater than the min_hit_length. If not, it is a short hit and is too weak.

If the "hit_ext" module FIG. 18 tells the "q_colour" module FIG. 17 that the hit was not a weak one, then the "q_colour" module determines whether the current hit is long enough 398 by calling the "colour" module FIG. 19. The "colour" module FIG. 19 performs query_colour modification by the hit data, starting at pos_query and described by mismatch_location_ahead and mismatch_location_behind. After the variables to be used in this module are defined, variable isw_print (which is the switch indicating the hit length) is initialized to zero 430. The cur_length is then set equal to the length of the extending hit 431 (mismatch_location_behind[i] + mismatch_location_ahead[j]-1). Next, if cur_length is greater than or equal to the min_hit_length 432 (i.e.,the minimum considered probe size), the hit is considered long and isw_print is set equal to two 433. The value of isw_print is then returned 434 to the "q_colour" module FIG. 17.

If the length of the extending hit is longer than the min_hit_length, the hit is considered long 399. Otherwise, the hit is considered short. If the hit is short, nothing more is done to the current hit and the module begins again. If, on the other hand, the hit is considered long 399, the "q_colour" module FIG. 17 prints the current extended hit 400. The current extended hit can be printed in ASCII, printed in a binary file, or printed to a memory file. The "q_colour" module FIG. 17 then repeats until the end of the linked list is reached.

d. **Outputs**

The output of the k_diff program in the current implementation of this invention may be either a binary file containing the number of extended hits and the k_mismatch hit locations (see FIG. 20), or the output may be kept in memory without writing it to a file. See Section 1(d)(iv) for more detail.

3. Description of the H-Site Model Program

a. **Overview**

In this invention, the second hybridization strength model is termed the H-Site Model (see FIG. 2 for user selection of this model). One aspect of the H-Site Model uses a generalization of an experimental formula in general usage. The formula used in the H-Site Model is an expression of the fact that melting temperature Tm is a function of both probe length and percent of GC content. This basic formula has been modified in this invention to account for the presence of mismatches. Each percent of mismatch reduces the melting temperature Tm by an average of 1.25 degrees (2 degrees C for an AT mismatch, and 4 degrees C for a GC mismatch).

In addition, this implementation of the invention does some preliminary preprocessing of the GenBank database to sort out and select the cDNA sequences. This is done by locating a keyword (in this case CDS) in each GenBank record. No other programs currently available allow for this combination of functions as far as the inventors are aware.

There are a number of modules in the present embodiment of the H-Site Model contained in this invention. Each step of the processing involved in the H-Site Model is more fully explained below, and is accompanied by detailed flow charts.

b. **Inputs**

There are two basic user-selected inputs for the H-Site Model (see FIG. 2C): 1) the melting temperature Tm 22 for which probes are being designed (i.e., the melting temperature that corresponds to a particular experiment or condition the user desires to simulate); and 2) the nucleation threshold 23, which is the number of base pairs constituting a nucleation site. The user is also required to select the 1) target species 11 gene sequence(s) (DNA, mRNA or cDNA) for which probes are being designed; 2) the preparation 12 of all sequences with which hybridizations are to be calculated; and 3) the probe output file 13. The preparation file is the most important, as discussed below.

c. **Organization of the H-Site Model Program**

The current implementation of the H-Site Model program of this invention is distributed between five files containing numerous modules. The main file is designated by the inventors as "ds.cpp" in its uncompiled version. This file provides overall control to the entire invention. It is divided into six sections. Section 0 defines and manipulates global variables. Section 1 controls general variable definition and initialization (including the arrays and memory blocks). It also reads and writes buffers for user input selections, and constructs multi buffers.

Section 2 sets up and initializes various "snippet" variables (see section below for a complete definition of the term snippet), converts base pair characters to a representation that is 96 base pairs long and to ASCII base pair strings, and performs other sequence file manipulation such as comparing snippets. This section also reads the sequence format file, reads base pairs, checks for and extracts sequence identification information (such as ORIGIN and LOCUS) and filters out sequences beginning with numbers.

Section 3 involves preparation file manipulation. This section performs the preprocessing on the PRP file discussed above. It also merges and sorts the snippet files, creates a PRP file and sorts it, and outputs the sorted snippets. Next, this section streams through the PRP file.

Section 4 contains the essential code for H-Site Model processing (see FIGS. 21 through 23 for details, discussed below). Streams are set up, and then RIBI comparisons are performed for hybridizations (see file "ribi.cpp"for definitions of RIBI search techniques). Next, probes are generated, binding strength is converted to melting temperature, and hybridizations are calculated and stored (including hybridization strength). Lastly, other H-Site calculations are performed.

Section 5 is concerned with formatting and presenting diagnostic and user file (test.out, test1.out, and test2.out files) output. This section also handles the graphing functions (the MPSD diagram in particular). In addition, this section calculates the hairpin characteristics for the H-Site Model candidate probes.

The second H-Site Model file, designated as "ds.h"defines data variables and structures. Section 1 of this file concerns generic data structures (including memory blocks and arrays, and file inputs and outputs). Section 2 defines the variables and structures used with sequences, probes and hybridizations. Section 3 defines variables and structures concerned with protocols (i.e., function prototypes, graphing, etc.).

The third H-Site Model file, designated as "funcdoc.txt",contains very detailed documentation for this implementation of the H-Site Model program. Numerous variables and structures are also defined. The flow of the program is clearly shown in this file.

The fourth H-Site Model file, designated as "ribi.h" handles the sequence comparisons. The fifth and last H-Site Model file, designated as "ribi.cpp",performs internal B-Tree indexing. Definitions of Red-black Internal Binary Index (RIBI) searching are found in this file. Definitions are also included for the concepts keyed set, index, binary tree, internal binary index, paths, and red-black trees. Implementation notes are also included in this file.

d. **Processing**

Implementation of the H-Site Model in this invention is done in three stages. First, the invention creates the preparation (PRP) file, which contains all relevant information from the sequence database. This is the preprocessing stage discussed above. Next, the target is prepared by the program. Lastly, the invention calculates the MPSD data using the PRP file and target sequence to find probes.

i. Creation of the Preprocessed Preparation File

FIG. 21. Step 1: The program first opens the sequence database for reading into memory 461, 462. Step 2: Next, as sequence base pairs are read in 462, "snippets" are saved to disk 463, along with loci information. A snippet is a fixed-length subsequence of a preparation sequence. The purpose of snippets is to allow the user to examine a small portion of a preparation sequence together with its surrounding base pairs. Snippets in the implementation of this invention are 96 base pairs long (except for snippets near the end or beginning of a sequence, which may have fewer base pairs). The "origin" of the snippet is in position 40. For snippets taken near the beginning of a sequence, some of the initial 40 bases are undefined. For snippets near the end of a sequence, some of the final 55 bases are undefined. Snippets are arranged in the preparation file (PRP) in sorted order (lexicographical order beginning at position 40). In this invention, the term "lexicographical order" means a preselected order, such as alphabetical, numeric or alphanumeric. In order to conserve space, snippets are only taken at every 4th position of the preparation sequence.

Step 3: The snippets are merge sorted 464 to be able to search quickly for sequences which pass the "screen", discussed below. Step 4: The merged file is prepended with identifiers for the sources of the snippets 465. This is done to identify the loci from which hybridizations arise.

ii. Target Preparation

FIG. 22. Step 1: The target sequence file is opened 471 and read into memory 472. For each position in the target mRNA, the probe defined at that starting position is the shortest subsequence starting at that position whose hybridization strength is greater than the user specified melting temperature Tm. Typically, the probes are of

length 18 to 50. Step 2: Four lists of "screens" are formed 473, 474, 475, each shifted by one base pair 475 to correspond to the fact that snippets are only taken at every four base pairs. A screen is a subsequence of the target mRNA of length equal to the screening threshold specified by the user. The screens are then indexed 476 and sorted in memory 477.

iii. Calculation of the MPSD Data

FIG. 23. Step 3: This step is the heart of the process. Step 3a: The program streams through the following five items in sync, examining them in sequential order: the snippet file and the four lists of screens 481-484. Step 3b: Each snippet is compared to a screen 485. Step 3c: If the snippet does not match, whichever stream is behind is advanced 486 and Step 3b is repeated. If the snippet does match, Step 4 is performed.

Step 4: If a snippet and a matching screen were found in Step 3b 487, the hybridization strength of the binding between the sequence containing the snippet and all of the probes containing the screen is calculated (see Step 5). Double counting is avoided by doing this only for the first matched screen containing the probe. Each pair of bases is examined and assigned a numerical binding strength. An AT pair would be assigned a lower binding strength than a GC pair because AT pairs have a lower melting temperature Tm. The process is explained more fully below at Step 5b.

Step 5: The hybridization strengths between sequence and all the probes containing it are calculated using a dynamic programming process. The process is as follows: Step 5a: Begin at the position of the first probe containing the given screen but not containing any other screens which start at an earlier position and also match the sequence. This is done to avoid double counting. Two running totals are maintained: a) boundStrength, which represents the hybridization strength contribution which would result if the sequence and probe were to match exactly for all base pairs to the right of the current position, and b) unboundStrength, which represents the strength of the maximally binding region. Step 5b: At each new base pair, the variable boundStrength is incremented by 71 if the sequence and probe match and the matched base pair is GC 489, incremented by 30 if the matched base pair is AT 490 (i.e., this number is about 42.25% of the first number 71), and decremented by 74.5 if there is not a match 488 (i.e., this number is about 5% larger than the first number 71). Step 5c: If the current boundStrength exceeds the current unboundStrength 491 (which was originally initialized to zero), a new binding region has been found, and unboundStrength is set equal to boundStrength 492. Step 5d: If the current boundStrength is negative, boundStrength is reset to zero 493. Step 5e: If the current position is at the end of a probe, the results (the hybridization strengths) are tallied for that probe. Step 5f: If the current position is at the end of the last probe containing the screen, the process stops.

Step 6: A tally is kept of the number and melting temperature of the matches for each candidate probe, and the location of the best 20 candidates, using a priority queue (reverse order by hybridization strength number) 494. Step 7: A numerical "score" is kept for each preparation sequence by tallying the quantity exp (which can be expressed as Σe^{-Tm}) for each match 495, where Tm is the melting temperature for the "perfect" match, the probe itself. In other words, the probe hybridizes "perfectly" to its target.

Step 8: Hairpins are calculated by first calculating the complementary probe. In other words, the order of the bases in the candidate probe are reversed (CTATAG to GATATC), and complementary base pairs are substituted (A for T, T for A, G for C, and C for G, changing GATATC to CTATAG in the above example). Next, the variable representing the maximum hairpin length for a candidate probe is initialized to zero, as is the variable representing a hairpin's distance. For each offset, the original candidate probe and the complementary probe just created are then aligned with each other and compared. The longest match is then found. If any two matches have the same length, the one with the longest hairpin distance (i.e., the number of base pairs separating the match) is then saved.

Step 9: The preparation sequences are then sorted 496 and displayed in rank order, from best to worst 497. Step 10: The resulting MPSD, which includes all candidate probes, is then displayed on the screen. Step 11: The best 20 matches are also printed or displayed in rank order, as the user requests 497.

e. **Outputs**

The outputs of the H-Site Model as currently implemented in this invention are fully described in Section 1(d)(iv), above, and illustrated in FIGS. 4 through 6. Samples of the two output files created by the H-Site Model are shown in FIGS. 24A and 24B.

4. Description of the Mitsuhashi Probe Selection Diagram Processing

Once the Mitsuhashi Probe Selection Diagram (MPSD) data has been calculated by the H-Site Model program (see stage three and FIG. 23, discussed above), it is necessary to convert this data to pixel format and plot a graph. An overview of this process is shown in FIG. 25. First, the program calculates the output (x,y) ranges 500. Next, these are converted to a logarithmic scale 501. The values are then interpolated 502, and a bitmap is created 503. Lastly, the bitmap is displayed on the screen 504 in MPSD format (discussed above in section 1(e)(i)). A sample MPSD is shown in FIG. 4.

5. Description of the MatchInfo Window Processing

The ProbeInfo and MatchInfo windows are discussed in great detail in Section 1(e)(ii), and a sample of these windows is shown in FIG. 5. An overview of the processing involved in creating the MatchInfo portion of the window is given in the flow chart in FIG. 26. First, as the user moves the MPSD cursor 520 (seen as a vertical line bisecting the MPSD window), the program updates the position of the candidate probe shown under that cursor position 521. Next, based upon the candidate probe's position, the program updates the sequence 522 and hairpin information 523 for that probe. This updated information is then displayed in an updated match list 524, shown in the MatchInfo window.

The above described embodiments of the present invention are merely descriptive of its principles and are not to be considered limiting. The scope of the present invention instead shall be determined from the scope of the following claims including their equivalents.

WHAT IS CLAIMED IS:

1. A programmed computer system for designing optimal oligonucleotide sequences for use with a gene sequence data source comprising:

first input means for introducing user-selected gene sequence into the computer system;

memory means for storing user-selected gene sequence;

means for accessing gene sequence data from said gene sequence data source;

means for performing exact and inexact match modeling between gene sequences;

means for performing hybridization strength modeling on gene sequences;

means for selecting either of said modeling means; and

means for presenting the results of said modeling to present candidate oligonucleotide sequences.

2. A programmed computer system in accordance with Claim 1 wherein said means for performing exact and inexact match modeling utilizes said accessing means to introduce a user-selected set of gene sequence data and a user-selected set of target gene sequence data from said gene sequence data source into the computer system and said memory means to store said gene sequence data and said target gene sequence data and wherein said means for performing exact and inexact match modeling includes:

means for determining a minimum sequence length;

means for creating a look-up hash table and linked list in memory for each gene sequence in said gene sequence data and each of said target gene sequences;

means for calculating the minimum length of any matching gene subsequence of said gene sequence data and said target gene sequence data;

means for comparing each base pair character in each said target sequence stored in a hash table in memory to each base pair character of said gene sequence stored in a hash table in memory;

means for finding a matching seed by determining if the said comparison results in a matching gene subsequence of length equal to said calculated minimum length;

means for comparing base pair characters behind and ahead of said seed to determine if there exists an extended match of a subsequence of base pair characters of length greater than the calculated minimum length, resulting in a current hit sequence;

means for calculating whether said current hit sequence is longer than said minimum sequence length, resulting in a current candidate oligonucleotide sequence;

means for storing said current candidate oligonucleotide sequence; and

wherein said presenting means provides said current candidate oligonucleotide sequence to the user.

3. A programmed computer system in accordance with Claim 2 wherein said computer system includes:

means for calculating the melting temperature for each candidate oligonucleotide sequence;

means for tracking the number and melting temperature of the matches for each candidate oligonucleotide sequence;

means for tracking the location of a set number of the best candidate oligonucleotide sequences; and

wherein said presenting means is operative to present said additional results to the user; and

wherein said presenting means provides said melting temperature to the user.

4. A programmed computer system in accordance with Claim 2 wherein said computer system includes:

means for determining the length of sequences from said target gene sequence data.

5. A programmed computer system in accordance with Claim 2 wherein said computer system includes:

means for determining the length of sequences from said set of gene sequence data.

6. A programmed computer system in accordance with Claim 2 wherein said computer system includes:

means for copying the LOCUS name for each said gene sequence into said memory means; and

means for linking said LOCUS name with each said gene sequence.

7. A programmed computer system in accordance with Claim 2 wherein said means for performing exact and inexact match modeling utilizes said accessing means to introduce a user-selected minimum sequence length from said gene sequence data source into the computer system and said memory means to store said minimum sequence length.

8. A programmed computer system in accordance with Claim 2 wherein said computer system includes:

means for calculating the melting temperature for each candidate oligonucleotide sequence;

means for tracking the number and melting temperature of the matches for each candidate oligonucleotide sequence;

means for tracking the location of a set number of the best candidate oligonucleotide sequences employing a priority queue by sorting said candidate oligonucleotide sequences in reverse order and sorting said candidate oligonucleotide sequences by hybridization strength;

wherein said presenting means is operative to present said additional results to the user; and

wherein said presenting means provides said melting temperature to the user.

9. A programmed computer system in accordance with Claim 2 wherein said first input means in operative to introduce a user-selected maximum number of mismatches and a user-selected minimum candidate oligonucleotide sequence length into the computer system, and wherein said means for calculating the minimum length of any matching gene subsequence of said gene sequence data and said target gene sequence data comprises the steps of:

means for subtracting said maximum number of mismatches from said minimum candidate oligonucleotide sequence length to give a first result;

means for dividing said first result by said maximum number of mismatches plus one to give a second result;

means for incrementing said second result by one if the remainder is not equal to zero to give a third result; and

means for truncating said third result to an integer.

10. A programmed computer system in accordance with Claim 9 wherein said means for calculating the hairpin characteristics of said candidate oligonucleotide sequence comprises the steps of:

calculating a complementary sequence to the candidate oligonucleotide sequence by reversing the base pair order of the candidate oligonucleotide sequence and substituting complementary base pairs;

comparing each character of said original candidate oligonucleotide sequence and said complementary sequence;

finding the longest match between said original candidate oligonucleotide sequence and said complementary sequence; and

saving the match with the longest hairpin distance if any two matches have the same length;

means for storing hairpin characteristics; and

wherein said presenting means provides said hairpin characteristics to the user.

11. A programmed computer system in accordance with Claim 2 wherein said computer system includes a means for calculating the hairpin characteristics of said candidate oligonucleotide sequence.

12. A programmed computer system in accordance with Claim 2 wherein said means for preprocessing said set of target gene sequence data and said set of gene sequence data comprises the steps of:

searching for sequences without introns in said target gene sequences and said gene sequences;

extracting target gene sequences and gene sequences that do not contain introns; and

storing said extracted target gene sequences and gene sequences in memory.

13. A programmed computer system in accordance with Claim 1 wherein said means for performing hybridization strength modeling utilizes said first input means to introduce a user-selected screening threshold into the computer system and said accessing means to introduce a user-selected set of gene sequence data and a user-selected set of target gene sequence data from said gene sequence data source into the computer system, and said memory means to store said gene sequence data, said target gene sequence data and said screening threshold and wherein said means for performing hybridization strength modeling comprises:

means for preprocessing said target gene sequence data and said gene sequence data by selecting only those sequences without introns;

means for forming a preparation file of gene sequence fragments by cutting said target gene sequences into fixed length target gene subsequences and sorting said subsequences in lexicographical order;

means for merge sorting said gene sequences;

means for forming multiple lists of screens by forming lists of subsequences of the preparation file of length equal to said screening threshold;

means for indexing, sorting and storing said screens in said memory means;

means for sequentially comparing said preparation file gene sequences with each of said screens to design candidate oligonucleotide sequences;

means for calculating the hybridization strengths between a gene sequence and all candidate oligonucleotide sequences containing that gene sequence by accounting for Guanine-Cytosine (GC) and Adenine-Thymine (AT) base pair content of the gene sequence and the number of mismatches between said preparation file sequences and a said screen when said comparison results in a match;

means for preparing the candidate oligonucleotide sequence and hybridization strength for presentation to the user; and

wherein said presenting means provides the candidate oligonucleotide sequence and hybridization strength to the user.

14. A programmed computer system in accordance with Claim 13 wherein said computer system includes:

means for calculating the melting temperature for each candidate oligonucleotide sequence;

means for tracking the number and melting temperature of the matches for each candidate oligonucleotide sequence;

means for tracking the location of a set number of the best candidate oligonucleotide sequences;

means for preparing the melting temperature for presentation to the user; and

wherein said presenting means provides the melting temperature to the user.

15. A programmed computer system in accordance with Claim 14 wherein said means for calculating said candidate oligonucleotide sequence's melting temperature comprises:

solving the formula Tm = 81.5 - 16.6(log[Na]) - .63 %(formamide) + ((.41 (%(G + C)) - 600)/N), wherein log[Na] is the sodium concentration, %(G + C) is the fraction of matched base pairs which are G-C complementary, N is the sequence length and wherein the number of mismatches is equal to zero.

16. A programmed computer system in accordance with Claim 15 wherein said computer system includes:

means for reducing a candidate oligonucleotide probe's calculated melting temperature by a certain amount for each percent of mismatch between the candidate oligonucleotide sequence and a user-selected target gene sequence based upon the assumption that there are an equal number of GC and AT base pair mismatches.

17. A programmed computer system in accordance with Claim 16 wherein said means for reducing a candidate oligonucleotide sequence's calculated melting temperature comprises the steps of:

reducing said calculated melting temperature by 2 degrees Celsius if an AT mismatch exists; and reducing said calculated melting temperature by 4 degrees Celsius if a GC mismatch exists.

18. A programmed computer system in accordance with Claim 13 wherein said computer system includes:

means for assigning a numerical score to each said gene sequence; and

means for sorting said gene sequences in accordance with said numerical score.

19. A programmed computer system in accordance with Claim 13 wherein said means for performing hybridization strength modeling utilizes said accessing means for copying the LOCUS name for each said gene sequence into said memory means, and said memory means; and

means for prepending said gene sequence with said LOCUS name.

20. A programmed computer system in accordance with Claim 13 wherein four lists of screens are formed by said list forming means.

21. A programmed computer system in accordance with Claim 13 wherein said computer system includes a means of shifting each screen by at least one base pair as it is formed by said list forming means.

22. A programmed computer system in accordance with Claim 13 wherein said computer system includes:

means for calculating the melting temperature for each candidate oligonucleotide sequence;

means for tracking the number and melting temperature of the matches for each candidate oligonucleotide sequence;

means for tracking the location of a set number of the best candidate oligonucleotide sequences employing a priority queue by sorting said candidate oligonucleotide sequences in reverse order and sorting said candidate oligonucleotide sequences by hybridization strength;

means for preparing the melting temperature for presentation to the user; and wherein said presenting means provides the melting temperature to the user.

23. A programmed computer system in accordance with Claim 13 wherein said computer system includes:

means for assigning a numerical score to each said gene sequence by tallying the quantity "exp" where "exp" = Σe^{-Tm} and wherein Tm is the melting temperature for the said gene sequence; and

means for sorting said gene sequences in accordance with said numerical score.

24. A programmed computer system in accordance with Claim 13 wherein said means for calculating the hybridization strengths between a gene sequence and all candidate oligonucleotide sequences containing that gene sequence comprises the steps of:

accessing gene sequence data from said gene sequence data source;

comparing base pairs of a first gene sequence and a second gene sequence to determine if a match exists;

incrementing said first gene sequence's bound strength by some first number if a base pair character in said first gene sequence and said second gene sequence match and the matched base pair is equal to a combination of the bases Guanine (G) and Cytosine (C);

incrementing said first gene sequence's bound strength by some second number if a base pair character in said first gene sequence and said second gene sequence match and the matched base pair is equal to a combination of the bases Adenine (A) and Thymine (T);

decrementing said first gene sequence's bound strength by a third number if there is no match in base pairs between said first gene sequence and said second gene sequence;

comparing said first gene sequence's bound strength to said first gene sequence's unbound strength;

setting said first gene sequence's unbound strength equal to its bound strength if said first gene sequence's bound strength is greater than said first gene sequence's unbound strength; and resetting said first gene sequence's bound strength to zero if said first gene sequence's unbound strength is less than zero.

25. A programmed computer system in accordance with Claim 24 wherein said first and second numbers are greater than zero.

26. A programmed computer system in accordance with Claim 24 wherein said second number is in the order of 42% of said first number.

27. A programmed computer system in accordance with Claim 24 wherein said third number is in the order of 5% larger than said first number.

28. A programmed computer system in accordance with Claim 13 wherein said computer system includes a means for calculating the hairpin characteristics of said candidate oligonucleotide sequence;

means for preparing the hairpin characteristics for presentation to the user; and

wherein said presenting means provides the hairpin characteristics to the user.

29. A programmed computer system in accordance with Claim 28 wherein said means for calculating the hairpin characteristics of said candidate oligonucleotide sequence comprises the steps of:

calculating a complementary sequence to the candidate oligonucleotide sequence by reversing the base pair order of the candidate oligonucleotide sequence and substituting complementary base pairs;

comparing each character of said original candidate oligonucleotide sequence and said complementary sequence;

finding the longest match between said original candidate oligonucleotide sequence and said complementary sequence; and

saving the match with the longest hairpin distance if any two matches have the same length;

means for preparing the hairpin characteristics for presentation to the user; and wherein said presenting means provides the hairpin characteristics to the user.

30. A programmed computer system in accordance with Claim 13 wherein said fixed-length subsequences are calculated by a method comprising the steps of:

locating the origin of said subsequence in a set position of said target gene sequence in said preparation file;

cutting a subsequence that is a fixed-length long every preselected number of positions of said target gene sequence in said preparation file; and

sorting said subsequences in said preparation file in lexicographical order beginning at a set position.

31. A programmed computer system in accordance with Claim 30 wherein the origin of said subsequence is located at position 40 of said target sequence in said preparation file.

32. A programmed computer system in accordance with Claim 13 wherein said fixed-length subsequences are calculated by a method comprising the steps of:

locating the origin of said subsequence in the 40th position of said target gene sequence in said preparation file;

cutting a subsequence that is 96 base pairs long of said target gene sequence in said preparation file; and

sorting said subsequences in said preparation file in lexicographical order beginning at a set position.

33. A programmed computer system in accordance with Claim 13 wherein said computer system includes means for prepending said preparation file subsequences with identifiers for the sources of each subsequence.

34. A programmed computer system in accordance with Claim 1 wherein said presenting means to provide the results of said matching and modeling to display candidate oligonucleotide sequences includes means for displaying in multiple dimensions the gene sequences which result from the comparisons and calculations characterized in that said display format exhibits

the starting position of each candidate oligonucleotide sequence in one dimension;

the specificity of a candidate oligonucleotide sequence's hybridization with the target gene sequence in a second dimension; and

superimposed melting temperatures of gene sequences in contrasting presentations in at least an apparent third dimension.

35. A programmed computer system in accordance with Claim 34 wherein said display further includes a cursor moveable along one dimension of said display that selects a position for an expansion of data representing the homology between the candidate oligonucleotide sequences and said gene sequence data; and

wherein said display is operative to display in alphanumeric form the homology between the candidate oligonucleotide sequences and said gene sequence data.

36. A programmed computer system in accordance with Claim 34 wherein said display is further operative to provide an expansion of data including presenting

false hybridizations at various melting temperatures for all candidate oligonucleotide sequences;

the location of each false hybridization;

a candidate oligonucleotide sequence's starting position; and

hairpin characteristics of each candidate oligonucleotide sequence.

37. A programmed computer system in accordance with Claim 34 wherein said display format data is outputted to a printing means.

38. A programmed computer system in accordance with Claim 34 wherein said display format data is saved to a data file.

39. A programmed computer system in accordance with Claim 34 wherein said display format data is exported to another computer system.

40. A programmed computer system in accordance with Claim 34 wherein said display further includes a cursor moveable along one dimension of said display that selects a position for an expansion of data representing the homology between the candidate oligonucleotide sequences and said gene sequence data; and

wherein said moveable cursor may be positioned by the user to select and save particular candidate oligonucleotide sequence information; and

wherein said display is operative to display in alphanumeric form the homology between the candidate oligonucleotide sequences and said gene sequence data.

41. A programmed computer system in accordance with Claim 40 wherein said method of selecting and saving particular candidate oligonucleotide sequence information comprises capturing candidate oligonucleotide sequence information at the user-selected point and storing said information in said memory means.

42. A programmed computer system in accordance with Claim 41 wherein said user-selected candidate oligonucleotide sequence information is exported to another computer system.

43. A programmed computer system in accordance with Claim 34 wherein said means for displaying comprises the steps of:

calculating display output ranges;
converting said output ranges to a logarithmic scale;
interpolating said converted values;
creating a bitmap of said interpolations; and
displaying said bitmap on a display device.

44. A programmed computer system in accordance with Claim 34 wherein said means for displaying comprises the steps of:

converting said result values to pixels;
filling a pixel array with said pixels;
performing a binary search into said pixel array;
determining the number of pixels per candidate oligonucleotide sequence to be displayed;

interpolating said pixels at the value of pixels per position minus one;
computing an array of said pixel array; and
plotting the results on a display device.

45. A programmed computer system in accordance with Claim 1 wherein said means for performing exact and inexact match modeling utilizes said accessing means to introduce a user-selected set of gene sequence data and a user-selected set of target gene sequence data from said gene sequence data source into the computer system and said memory means to store said gene sequence data and said target gene sequence data and wherein said means for performing exact and inexact match modeling includes:

means for determining a minimum sequence length;

means for creating a look-up hash table and linked list in memory for each gene sequence in said gene sequence data and each of said target gene sequences;

means for calculating the minimum length of any matching gene subsequence of said gene sequence data and said target gene sequence data;

means for transforming base characters in each said target sequence and in each said gene sequence into numeric digits;

means for comparing each base pair digit in each said target sequence stored in a hash table in memory to each base pair digit of said gene sequence stored in a hash table in memory;

means for finding a matching seed by determining if the said comparison results in a matching gene subsequence of length equal to said calculated minimum length;

means for comparing base pair digits behind and ahead of said seed to determine if there exists an extended match of a subsequence of base pair digits of length greater than the calculated minimum length, resulting in a current hit sequence;

means for calculating whether said current hit sequence is longer than said minimum sequence length, resulting in a current candidate oligonucleotide sequence;

means for storing said current candidate oligonucleotide sequence; and

wherein said presenting means provides said current candidate oligonucleotide sequence to the user.

46. A programmed computer system for designing candidate oligonucleotide sequences for use with a gene sequence data source including:

first input means for introducing user-selected gene sequence, design, model and presentation criteria and a user-specified sequence length into the computer system;

memory means for storing said gene sequence, design, model and presentation criteria and said sequence length;

means for accessing gene sequence data from said gene sequence data source;

wherein said accessing means is operative to introduce a user-selected set of gene sequence data and a user-selected set of target gene sequence data from said gene sequence data source into the computer system;

wherein said criteria are used for comparison of gene sequence data and target gene sequence data;

means for comparing said gene sequences against said target gene sequences employing said criteria;

means for calculating candidate oligonucleotide sequences of said sequence length that are either common to a pool of user-specified gene sequences or specific to a particular user-specified gene sequence;

means for calculating the homology between the candidate oligonucleotide sequences and said gene sequence data;

means for calculating a candidate oligonucleotide sequence's hairpin characteristics;

means for displaying in multiple dimensions the gene sequences which result from the comparisons and calculations characterized in that said display format exhibits:

the starting position of each candidate oligonucleotide sequence in one dimension;

a candidate oligonucleotide sequence's specificity to the target gene sequence in a second dimension; and

superimposed melting temperatures of gene sequences in contrasting presentations in at least an apparent third dimension;

wherein said display further includes a cursor moveable along one dimension of said display that selects a position for an expansion of data representing the homology between the candidate oligonucleotide sequences and said gene sequence data;

wherein said display is operative to display in alphanumeric form the homology between the candidate oligonucleotide sequences and said gene sequence data; and

wherein said display is operative to provide an expansion of data including presenting

false hybridizations at various melting temperatures for all candidate oligonucleotide sequences;

the location of each false hybridization;

a candidate oligonucleotide sequence's starting position; and

hairpin characteristics of each candidate oligonucleotide sequence.

47. A method for designing candidate oligonucleotide sequences by performing exact and inexact match modeling for use with a gene sequence data source comprising the steps of:

introducing user-selected gene sequence into a computer system;

accessing gene sequence data from said gene sequence data source;

storing user-selected gene sequence in the memory of the computer system;

accessing the gene sequence source to introduce the user-selected set of gene sequence data and a user-selected set of target gene sequence data from said gene sequence data source into the computer system;

storing said gene sequence data and said target gene sequence data in the memory of the computer system;

determining a minimum sequence length;

creating a look-up hash table and linked list in memory for each gene sequence in said gene sequence data and each of said target gene sequences;

calculating the minimum length of any matching gene subsequence of said gene sequence data and said target gene sequence data;

comparing each base pair character in each said target sequence stored in a hash table in memory to each base pair character of said gene sequence stored in a hash table in memory;

determining a matching seed by determining if the said comparison results in a matching gene subsequence of length equal to said calculated minimum length;

comparing base pair characters behind and ahead of said seed to determine if there exists an extended match of a subsequence of base pair characters of length greater than the calculated minimum length, resulting in a current hit sequence;

calculating whether said current hit sequence is longer than said minimum sequence length, resulting in a current candidate oligonucleotide sequence;

storing said current candidate oligonucleotide sequence in the memory of the computer system; and

presenting a representation of said current candidate oligonucleotide sequence to the user.

48. A method in accordance with Claim 47 wherein said method includes the steps for performing additional calculations for each candidate oligonucleotide probe, said additional calculations comprising:

calculating the melting temperature for each candidate oligonucleotide sequence;

tracking the number and melting temperature of the matches for each candidate oligonucleotide sequence;

tracking the location of a set number of the best candidate oligonucleotide sequences; and

presenting said additional results to the user.

49. A method in accordance with Claim 47 wherein said method includes the step of transforming base characters into numeric digits.

50. A method in accordance with Claim 47 wherein said method includes the step of determining the length of sequences from said target gene sequence data.

51. A method in accordance with Claim 47 wherein said method includes the step of determining the length of sequences from said set of gene sequence data.

52. A method in accordance with Claim 47 wherein said method includes the steps of:

copying the LOCUS name for each said gene sequence into the memory of the computer system; and

linking said LOCUS name with each said gene sequence.

53. A method in accordance with Claim 47 wherein said method includes the steps of:

introducing a user-selected minimum sequence length into the computer system; and

storing said minimum sequence length in the memory of the computer system.

54. A method in accordance with Claim 47 wherein said method includes the steps for performing additional calculations for each candidate oligonucleotide probe, said additional calculations comprising:

calculating the melting temperature for each candidate oligonucleotide sequence;

tracking the number and melting temperature of the matches for each candidate oligonucleotide sequence;

tracking the location of a set number of the best candidate oligonucleotide sequences employing a priority queue by sorting said candidate oligonucleotide sequences in reverse order and sorting said candidate oligonucleotide sequences by hybridization strength; and

presenting said additional results to the user.

55. A method in accordance with Claim 47 wherein said step for calculating the minimum length of any matching gene subsequence comprises:

introducing a user-selected maximum number of mismatches and a user-selected minimum candidate oligonucleotide sequence length into the computer system;

subtracting said maximum number of mismatches from said minimum candidate oligonucleotide sequence length to give a first result;

dividing said first result by said maximum number of mismatches plus one to give a second result;

incrementing said second result by one if the remainder is not equal to zero to give a third result; and

truncating said third result to an integer.

56. A method in accordance with Claim 47 wherein said method includes the step of calculating the hairpin characteristics of said candidate oligonucleotide sequence.

57. A method in accordance with Claim 47 wherein said method includes the step of calculating the hairpin characteristics of said candidate oligonucleotide sequence comprising:

calculating a complementary sequence to the candidate oligonucleotide sequence by reversing the base pair order of the candidate oligonucleotide sequence and substituting complementary base pairs;

comparing each character of said original candidate oligonucleotide sequence and said complementary sequence;

finding the longest match between said original candidate oligonucleotide sequence and said complementary sequence; and

saving the match with the longest hairpin distance if any two matches have the same length.

58. A method for designing candidate oligonucleotide sequences by performing hybridization strength modeling for use with a gene sequence data source comprising the steps of:

introducing user-selected gene sequence and a user-selected screening threshold into a computer system;

storing user-selected gene sequence and said screening threshold in the memory of the computer system;

accessing the gene sequence source to introduce the user-selected set of gene sequence data and a user-selected set of target gene sequence data from said gene sequence data source into the computer system;

storing said gene sequence data and said target gene sequence data in the memory of the computer system;

preprocessing said target gene sequence data and said gene sequence data by selecting only those sequences without introns;

forming a preparation file of gene sequence fragments by cutting said target gene sequences into fixed length target gene subsequences and sorting said subsequences in lexicographical order;

merge sorting said gene sequences;

forming multiple lists of screens by forming lists of subsequences of the preparation file of length equal to said screening threshold;

indexing and sorting said screens in memory;

storing said screens in the memory of the computer system;

sequentially comparing said preparation file gene sequences with each of said screens to design candidate oligonucleotide sequences;

calculating the hybridization strengths between a gene sequence and all candidate oligonucleotide sequences containing that gene sequence by accounting for Guanine-Cytosine (GC) and Adenine-Thymine (AT) base pair content of the gene sequence and the number of mismatches between said preparation file sequences and a said screen when said comparison results in a match;

preparing the candidate oligonucleotide sequence and hybridization strength for presentation to the user; and

presenting the candidate oligonucleotide sequence and hybridization strength to the user.

59. A method in accordance with Claim 58 wherein said method includes the steps for performing additional calculations for each candidate oligonucleotide probe, said additional calculations comprising:

calculating the melting temperature for each candidate oligonucleotide sequence;

tracking the number and melting temperature of the matches for each candidate oligonucleotide sequence;

tracking the location of a set number of the best candidate oligonucleotide sequences; and

presenting said additional results to the user.

60. A method in accordance with Claim 58 wherein the step for preparing the candidate oligonucleotide sequence for presenting to the user comprises:

assigning a numerical score to each said gene sequence;

sorting said gene sequences in accordance with said numerical score; and

displaying a representation of the resulting candidate oligonucleotide sequence and said gene sequences.

61. A method in accordance with Claim 58 wherein said method includes the steps of:

copying the LOCUS name for each said gene sequence into the memory of the computer system; and

prepending said gene sequence with said LOCUS name.

62. A method in accordance with Claim 58 wherein the step for forming lists of screens produces four lists of screens.

63. A method in accordance with Claim 58 wherein said method includes a the step of shifting each screen by one base pair as it is formed.

64. A method in accordance with Claim 58 wherein said method includes the steps for performing additional calculations for each candidate oligonucleotide probe, said additional calculations comprising:

calculating the melting temperature for each candidate oligonucleotide sequence;

tracking the number and melting temperature of the matches for each candidate oligonucleotide sequence;

tracking the location of a set number of the best candidate oligonucleotide sequences employing a priority queue by sorting said candidate oligonucleotide sequences in reverse order and sorting said candidate oligonucleotide sequences by hybridization strength; and

presenting said additional results to the user.

65. A method in accordance with Claim 58 wherein said method for preparing the results for presenting to the user comprises:

assigning a numerical score to each said gene sequence by tallying the quantity "exp" where "exp" = Σe^{-Tm} and wherein Tm is the melting temperature for the said gene sequence;

sorting said gene sequences in order of the numerical score; and

displaying a representation of the resulting candidate oligonucleotide sequence and said gene sequences.

66. A method in accordance with Claim 58 for use with a gene sequence data source, programmed to determine hybridization strength comprising the steps of:

comparing base pairs of a first gene sequence and a second gene sequence to determine if a match exists;

incrementing said first gene sequence's bound strength by some first number if a base pair character in said first gene sequence and said second gene sequence match and the matched base pair is equal to a combination of the bases Guanine (G) and Cytosine (C);

incrementing said first gene sequence's bound strength by some second number if a base pair character in said first gene sequence and said second gene sequence match and the matched base pair is equal to a combination of the bases Adenine (A) and Thymine (T);

decrementing said first gene sequence's bound strength by a third number if there is no match in base pairs between said first gene sequence and said second gene sequence;

comparing said first gene sequence's bound strength to said first gene sequence's unbound strength;

setting said first gene sequence's unbound strength equal to its bound strength if said first gene sequence's bound strength is greater than said first gene sequence's unbound strength; and

resetting said first gene sequence's bound strength to zero if said first gene sequence's unbound strength is less than zero.

67. A method in accordance with Claim 66 wherein said first and second numbers are greater than zero.

68. A method in accordance with Claim 66 wherein said second number is in the order of 42% of said first number.

69. A method in accordance with Claim 66 wherein said second number is in the order of 5% larger than said first number.

70. A method in accordance with Claim 58 wherein said method includes the step of calculating the hairpin characteristics of said candidate oligonucleotide sequence.

71. A method in accordance with Claim 70 wherein the step of calculating the hairpin characteristics of said candidate oligonucleotide sequence includes the steps of:

calculating a complementary sequence to the candidate oligonucleotide sequence by reversing the base pair order of the candidate oligonucleotide sequence and substituting complementary base pairs;

comparing each character of said original candidate oligonucleotide sequence and said complementary sequence;

finding the longest match between said original candidate oligonucleotide sequence and said complementary sequence; and

saving the match with the longest hairpin distance if any two matches have the same length.

72. A method in accordance with Claim 58 wherein said fixed-length target gene subsequences are calculated by a method comprising the steps of:

locating the origin of said subsequence in a set position of said target gene sequence in said preparation file;

cutting a subsequence that is a fixed-length long every preselected number of positions of said target gene sequence in said preparation file; and

sorting said subsequences in said preparation file in lexicographical order beginning at a set position.

73. A method in accordance with Claim 72 wherein the origin of said subsequence is located at position 40 of said target sequence in said preparation file.

74. A method in accordance with Claim 58 wherein said fixed-length subsequences are calculated by a method comprising the steps of:

locating the origin of said subsequence in the 40th position of said target gene sequence in said preparation file;

cutting a subsequence that is 96 base pairs long of said target gene sequence in said preparation file; and

sorting said subsequences in said preparation file in lexicographical order beginning at a set position.

75. A method in accordance with Claim 58 wherein said method includes the step of prepending said preparation file subsequences with identifiers for the sources of each subsequence.

76. A method in accordance with Claim 58 wherein said method includes the step of calculating an candidate oligonucleotide sequence's melting temperature comprising:

solving the formula Tm = 81.5 - 16.6(log[Na]) - .63 %(formamide) + ((.41 (%(G + C)) - 600)/N);

wherein log[Na] is the sodium concentration, %(G + C) is the fraction of matched base pairs which are G-C complementary, N is the sequence length; and

wherein the number of mismatches is equal to zero.

77. A method in accordance with Claim 58 wherein said method includes the step for reducing a candidate oligonucleotide sequence's calculated melting temperature by a preselected amount for each percent of mismatch between the candidate oligonucleotide sequence and a user-selected target gene sequence based upon the assumption that there are an equal number of GC and AT base pair mismatches.

78. A method in accordance with Claim 58 wherein said method includes the step for reducing a candidate oligonucleotide sequence's calculated melting temperature by a preselected amount comprising the steps of:

reducing said calculated melting temperature by 2 degrees Celsius if an AT mismatch exists; and reducing said calculated melting temperature by 4 degrees Celsius if a GC mismatch exists.

79. A method for designing candidate oligonucleotide sequences for use with a gene sequence data source comprising the steps of:

introducing user-selected gene sequence and a user-specified sequence length into a computer system;

storing said gene sequence and said sequence length in the memory of the computer system;

accessing gene sequence data from said gene sequence data source;

accessing the gene sequence source to introduce the user-selected set of gene sequence data and a user-selected set of target gene sequence data from said gene sequence data source into the computer system;

comparing said gene sequences against said target gene sequences employing said criteria;

calculating candidate oligonucleotide sequences of said sequence length that are either common to a pool of user-specified gene sequences or specific to a particular user-specified gene sequence;

calculating the homology between the candidate oligonucleotide sequences and said gene sequence data;

displaying in multiple dimensions the gene sequences which result from the comparisons and calculations characterized in that said display format exhibits:

the starting position of each candidate oligonucleotide sequence in one dimension;

a candidate oligonucleotide sequence's specificity to the target gene sequence in a second dimension; and

superimposed melting temperatures of gene sequences in contrasting presentations in at least an apparent third dimension.

80. A method in accordance with Claim 79 wherein said method includes the step of calculating a candidate oligonucleotide sequence's hairpin characteristics.

81. A method in accordance with Claim 80 wherein said step of calculating hairpin characteristics for a gene sequence comprises:

calculating a complementary sequence to the said gene sequence by reversing the base pair order of the gene sequence and substituting complementary base pairs;

comparing each character of said original gene sequence and said complementary sequence;

finding the longest match between said original gene sequence and said complementary sequence; and

saving the match with the longest hairpin distance if any two matches have the same length.

82. A method in accordance with Claim 79 wherein the step of displaying further includes producing a cursor moveable along one dimension of said display that selects a position for an expansion of data representing the homology between the candidate oligonucleotide sequences and said gene sequence data; and

displaying in alphanumeric form the homology between the candidate oligonucleotide sequences and said gene sequence data.

83. A method in accordance with Claim 79 wherein said display format data is outputted to a printing means.

84. A method in accordance with Claim 79 wherein said display format data is saved to a data file.

85. A method in accordance with Claim 79 wherein said display format data is exported to another computer system.

86. A method in accordance with Claim 79 wherein the step of displaying further includes producing a cursor moveable along one dimension of said display that selects a position for an expansion of data representing the homology between the candidate oligonucleotide sequences and said gene sequence data;

positioning said moveable cursor to select and save particular candidate oligonucleotide sequence information; and

displaying in alphanumeric form the homology between the candidate oligonucleotide sequences and said gene sequence data.

87. A method in accordance with Claim 79 wherein the step of displaying further includes producing a cursor moveable along one dimension of said display that selects a position for an expansion of data representing the homology between the candidate oligonucleotide sequences and said gene sequence data;

positioning said moveable cursor to select and save particular candidate oligonucleotide sequence information;

capturing candidate oligonucleotide sequence information at the user-selected point and storing said information in said memory means; and

displaying in alphanumeric form the homology between the candidate oligonucleotide sequences and said gene sequence data.

88. A method in accordance with Claim 79 wherein said method of displaying comprises:

calculating display output ranges;

converting said output ranges to a logarithmic scale;

interpolating said converted values;

creating a bitmap of said interpolations; and

displaying said bitmap on a display device.

89. A method in accordance with Claim 79 wherein said method of displaying comprises:

converting said result values to pixels;

filling a pixel array with said pixels;

performing a binary search into said pixel array;

determining the number of pixels per candidate oligonucleotide sequence to be displayed;

interpolating said pixels at the value of pixels per position minus one;

computing an array of said pixel array; and

plotting the results on a display device.

90. A method to determine hybridization strength between two or more gene sequences for use with a gene sequence data source, comprising the steps of:

accessing gene sequence data from said gene sequence data source;

comparing base pairs of a first gene sequence and a second gene sequence to determine if a match exists;

incrementing said first gene sequence's bound strength by some first number if a base pair character in said first gene sequence and said second gene sequence match and the matched base pair is equal to a combination of the bases Guanine (G) and Cytosine (C);

incrementing said first gene sequence's bound strength by some second number if a base pair character in said first gene sequence and said second gene sequence match and the matched base pair is equal to a combination of the bases Adenine (A) and Thymine (T);

decrementing said first gene sequence's bound strength by a third number if there is no match in base pairs between said first gene sequence and said second gene sequence;

comparing said first gene sequence's bound strength to said first gene sequence's unbound strength;

setting said first gene sequence's unbound strength equal to its bound strength if said first gene sequence's bound strength is greater than said first gene sequence's unbound strength; and

resetting said first gene sequence's bound strength to zero if said first gene sequence's unbound strength is less than zero.

91. A method in accordance with Claim 90 wherein said first and second numbers are greater than zero.

92. A method in accordance with Claim 90 wherein said second number is in the order of 42% of said first number.

93. A method in accordance with Claim 90 wherein said third number is in the order of 5% larger than said first number.

94. A method of calculating the minimum length of any matching gene subsequence comprising:

introducing a user-selected maximum number of mismatches and a user-selected minimum candidate oligonucleotide sequence length;

subtracting said maximum number of mismatches from said minimum candidate oligonucleotide sequence length to give a first result;

dividing said first result by said maximum number of mismatches plus one to give a second result;

incrementing said second result by one if the remainder is not equal to zero to give a third result; and

truncating said third result to an integer.

95. A method of calculating hairpin characteristics for a gene sequence comprising:

calculating a complementary sequence to the said gene sequence by reversing the base pair order of the gene sequence and substituting complementary base pairs;

comparing each character of said original gene sequence and said complementary sequence;

finding the longest match between said original gene sequence and said complementary sequence; and

saving the match with the longest hairpin distance if any two matches have the same length.

96. A method of creating a preparation file from a user-selected set of target gene sequence data comprising:

cutting said target gene sequence data into fixed-length subsequences; and

storing said subsequences in a preparation file.

97. A method of creating a preparation file from a user-selected set of target gene sequence data comprising:

cutting said target gene sequence data into fixed-length subsequences in the order of 96 base pairs in length; and

storing said subsequences in a preparation file.

98. A method in accordance with Claim 97 wherein said fixed-length subsequences are calculated by a method comprising the steps of:

locating the origin of said subsequence in a set position of said target gene sequence in said preparation file;

cutting a subsequence that is a fixed-length long every preselected number of positions of said target gene sequence in said preparation file; and

sorting said subsequences in said preparation file in lexicographical order beginning at a set position.

99. A method in accordance with Claim 97 wherein said fixed-length subsequences are calculated by a method comprising the steps of:

locating the origin of said subsequence in a set position of said target gene sequence in said preparation file wherein the origin of said subsequence is located at position 40 of said target sequence in said preparation file;

cutting a subsequence that is a fixed-length long every preselected number of positions of said target gene sequence in said preparation file; and

sorting said subsequences in said preparation file in lexicographical order beginning at a set position.

100. A method in accordance with Claim 97 wherein said fixed-length subsequences are calculated by a method comprising the steps of:

locating the origin of said subsequence the 40th position of said target gene sequence in said preparation file;

cutting a subsequence that is 96 base pairs long of said target gene sequence in said preparation file; and

sorting said subsequences in said preparation file in lexicographical order beginning at a set position.

101. A method of forming lists of screens of target gene sequence data comprising:

introducing a user-selected screening threshold; and

forming subsequences of said target gene sequence data of length equal to a user-selected screening threshold.

102. A method of preprocessing a user-selected set of target gene sequence data comprising the steps of:

searching for sequences without introns in said target gene sequences; extracting target gene sequences that do not contain introns; and storing said extracted target gene sequences.

AMENDED CLAIMS

[received by the International Bureau on 4 April 1994 (04.04.94); original claim 69 amended; remaining claims unchanged (1 page)]

68. A method in accordance with Claim 66 wherein said second number is in the order of 42% of said first number.

69. A method in accordance with Claim 66 wherein said third number is in the order of 5% larger than said first number.

70. A method in accordance with Claim 58 wherein said method includes the step of calculating the hairpin characteristics of said candidate oligonucleotide sequence.

71. A method in accordance with Claim 70 wherein the step of calculating the hairpin characteristics of said candidate oligonucleotide sequence includes the steps of:

calculating a complementary sequence to the candidate oligonucleotide sequence by reversing the base pair order of the candidate oligonucleotide sequence and substituting complementary base pairs;

comparing each character of said original candidate oligonucleotide sequence and said complementary sequence;

finding the longest match between said original candidate oligonucleotide sequence and said complementary sequence; and

saving the match with the longest hairpin distance if any two matches have the same length.

72. A method in accordance with Claim 58 wherein said fixed-length target gene subsequences are calculated by a method comprising the steps of:

locating the origin of said subsequence in a set position of said target gene sequence in said preparation file;

cutting a subsequence that is a fixed-length long every preselected number of positions of said target gene sequence in said preparation file; and

sorting said subsequences in said preparation file in lexicographical order beginning at a set position.

73. A method in accordance with Claim 72 wherein the origin of said subsequence is located at position 40 of said target sequence in said preparation file.

FIG. 1

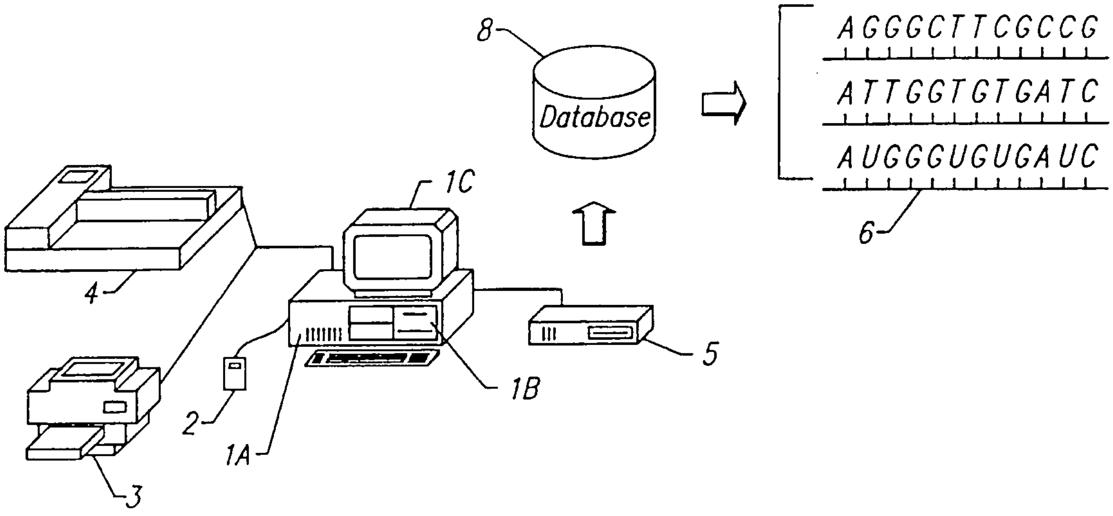
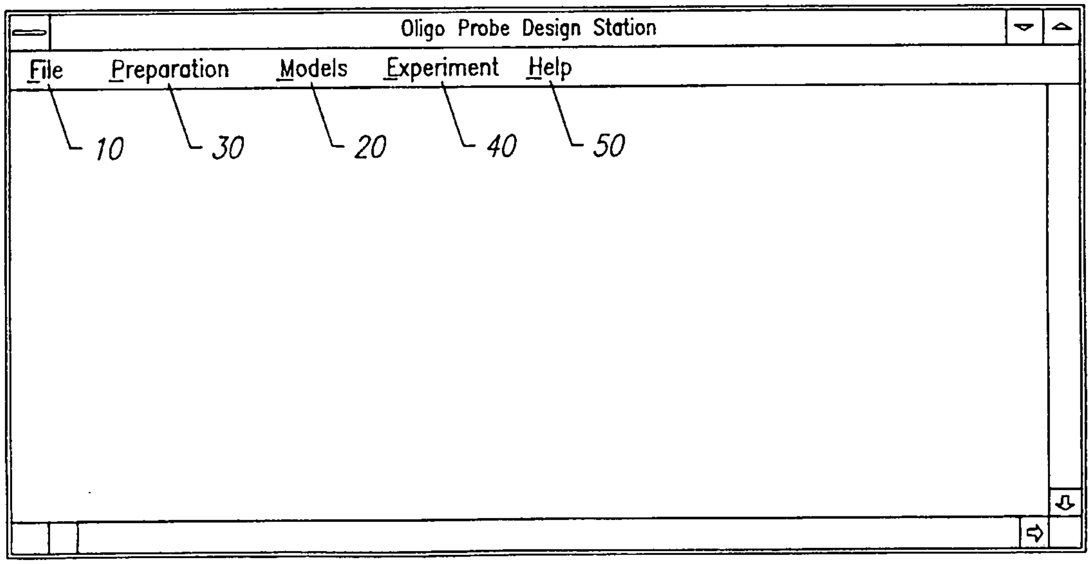

8
Database
AGGGCTTCGCCG
ATTGGTGTGATC
AUGGGUGUGAUC
6
1C
4
5
1B
2
1A
3

FIG. 2A


Oligo Probe Design Station
File
Preparation
Models
Experiment
Help
10
30
20
40
50

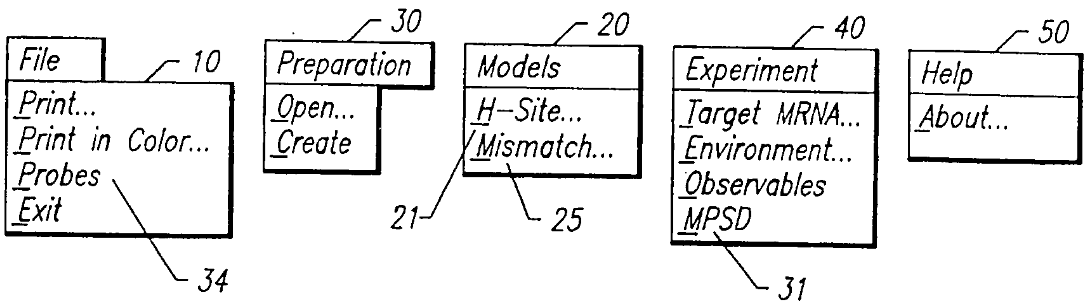

File
Print...
Print in Color...
Probes
Exit
10
34
Preparation
Open...
Create
30
Models
H-Site...
Mismatch...
20
21
25
Experiment
Target MRNA...
Environment...
Observables
MPSD
40
31
Help
About...
50

FIG. 2B

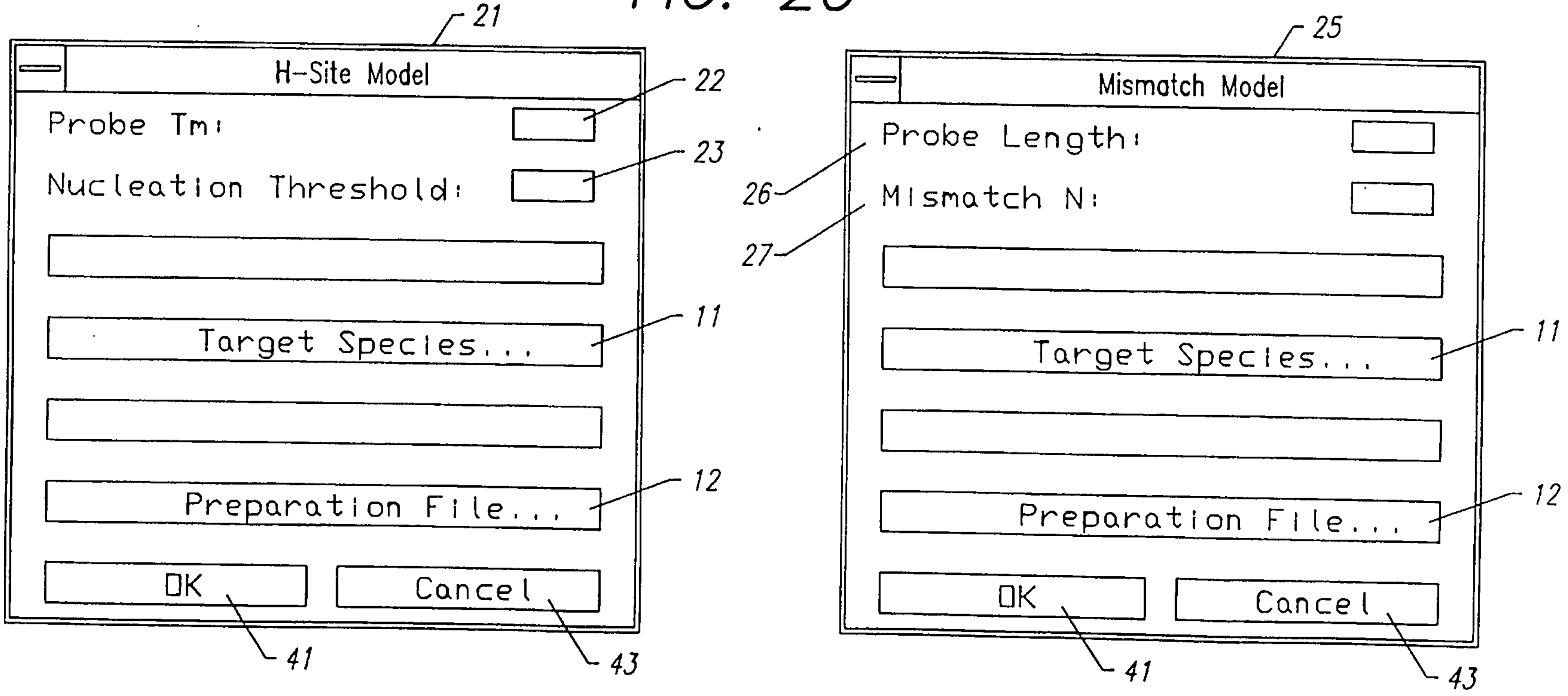

21
H-Site Model
Probe Tm:
Nucleation Threshold:
22
23
Target Species...
11
Preparation File...
12
OK
Cancel
41
43
25
Mismatch Model
Probe Length:
Mismatch N:
26
27
Target Species...
11
Preparation File...
12
OK
Cancel
41
43

FIG. 2C

FIG. 3

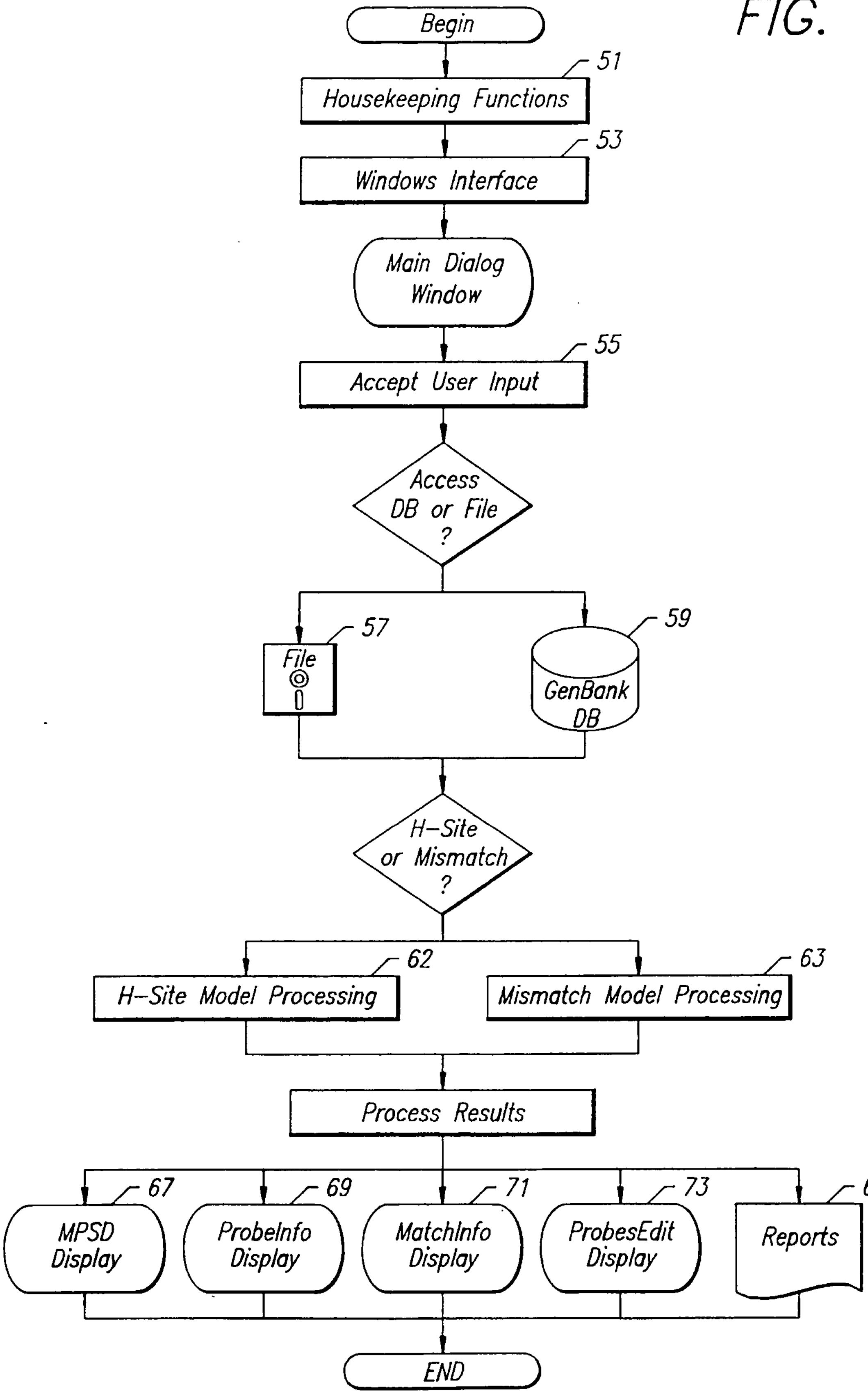

Begin
Housekeeping Functions
51
Windows Interface
53
Main Dialog Window
Accept User Input
55
Access DB or File ?
File
57
GenBank DB
59
H-Site or Mismatch ?
H-Site Model Processing
62
Mismatch Model Processing
63
Process Results
MPSD Display
67
ProbeInfo Display
69
MatchInfo Display
71
ProbesEdit Display
73
Reports
65
END

FIG. 4

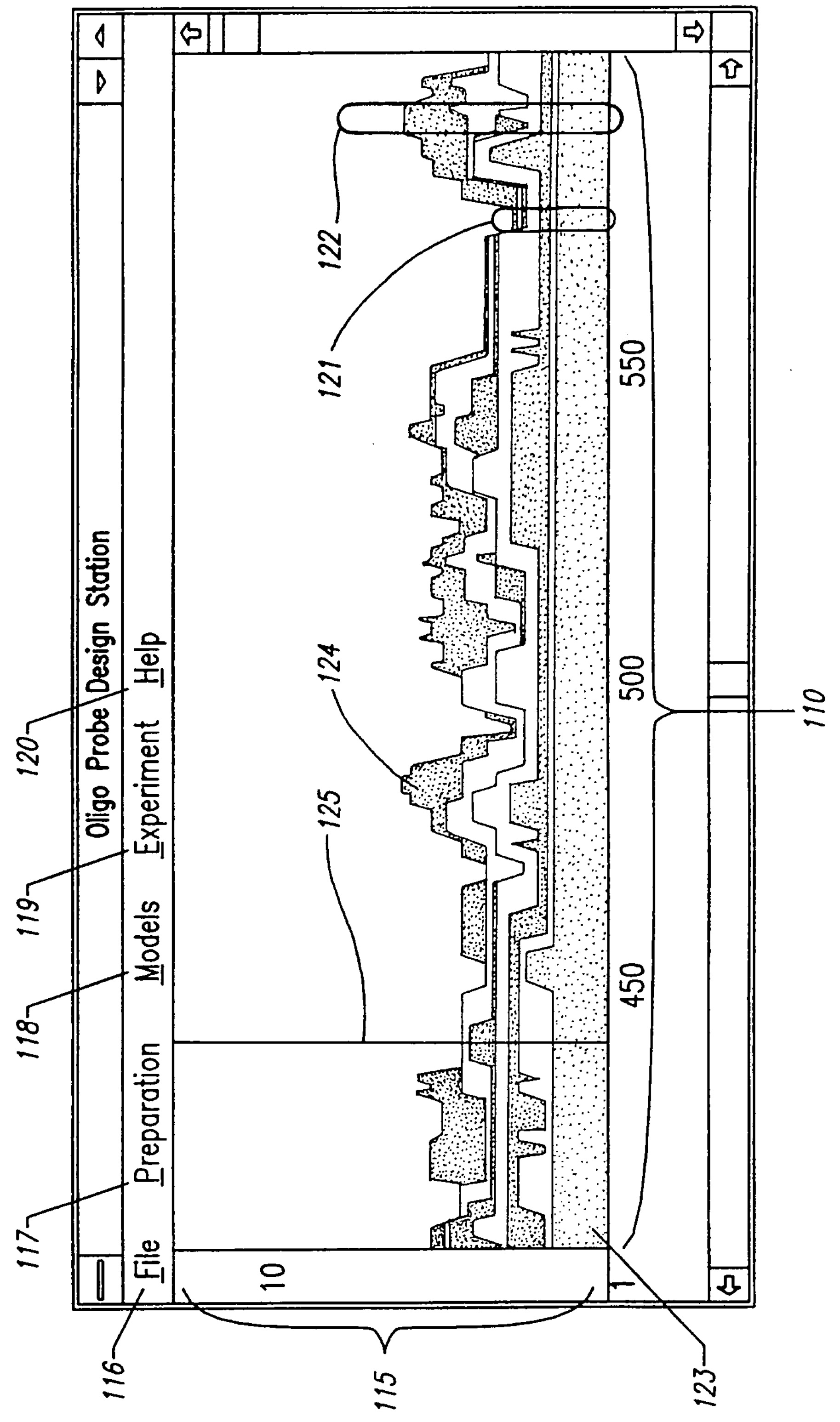
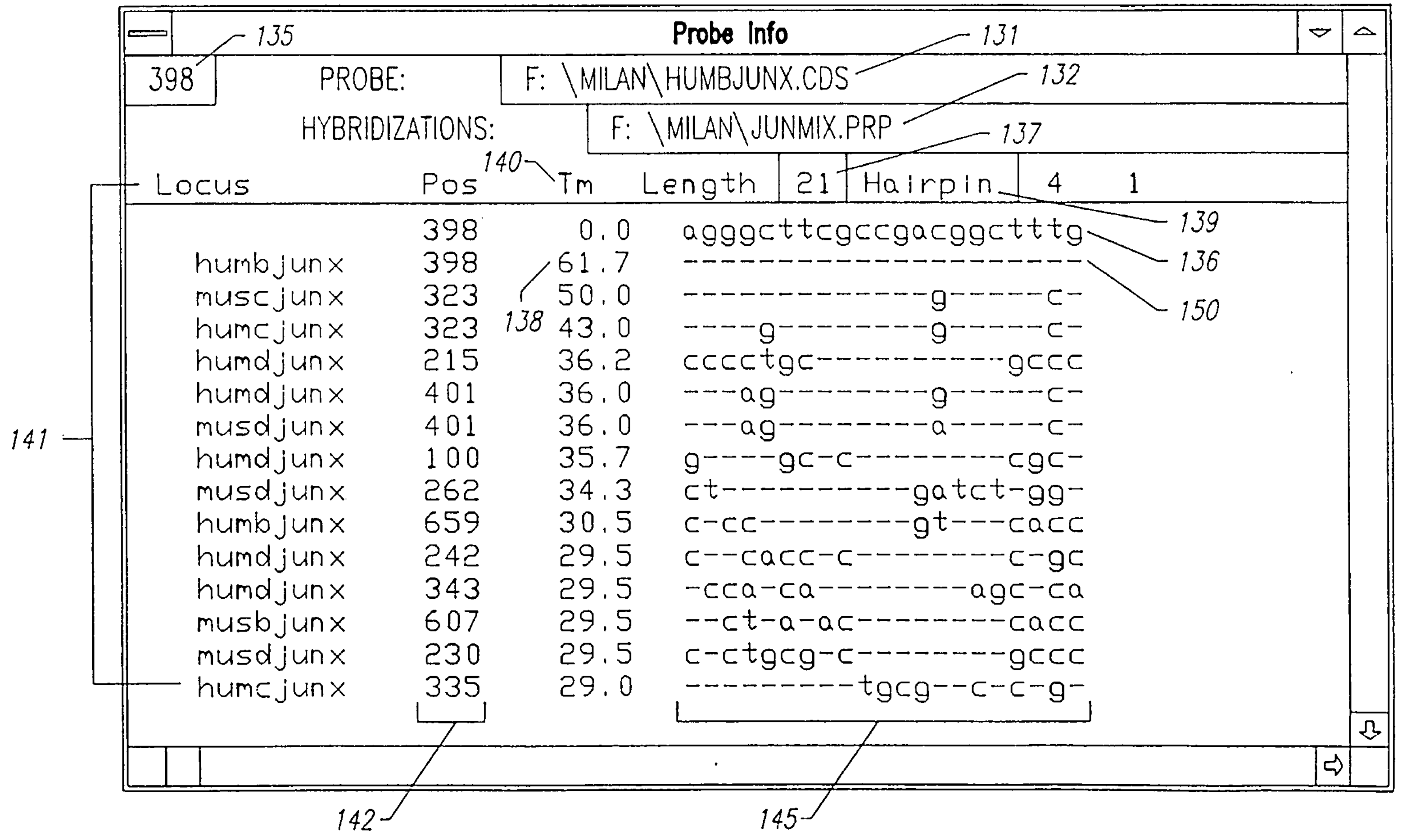
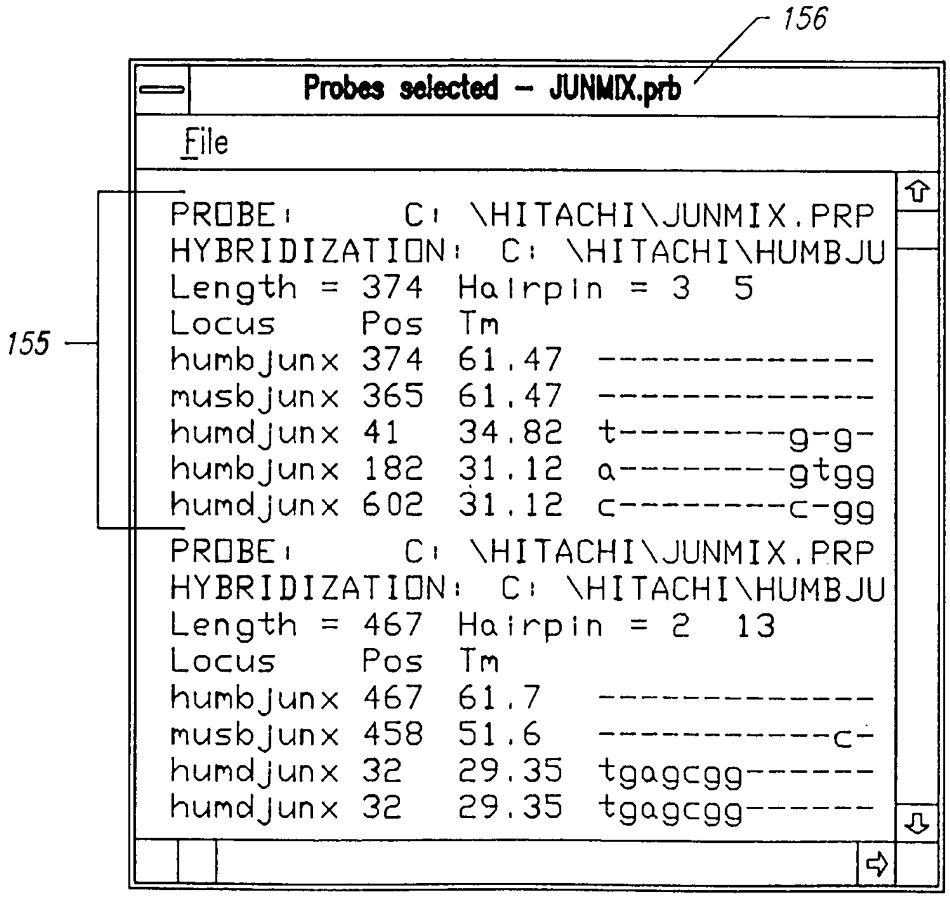

Oligo Probe Design Station
File
Preparation
Models
Experiment
Help
10
1
450
500
550
110
115
116
117
118
119
120
121
122
123
124
125

FIG. 5



```
                                   Probe Info
398          PROBE:         F: \MILAN\HUMBJUNX.CDS
           HYBRIDIZATIONS:      F: \MILAN\JUNMIX.PRP
Locus           Pos    Tm   Length | 21 | Hairpin | 4   1
                398    0.0  agggcttcgccgacggctttg
   humbjunx     398   61.7  ---------------------
   muscjunx     323   50.0  -------------g-----c-
   humcjunx     323   43.0  ----g--------g-----c-
   humdjunx     215   36.2  cccctgc----------gccc
   humdjunx     401   36.0  ---ag--------g-----c-
   musdjunx     401   36.0  ---ag--------a-----c-
   humdjunx     100   35.7  g----gc-c--------cgc-
   musdjunx     262   34.3  ct----------gatct-gg-
   humbjunx     659   30.5  c-cc--------gt---cacc
   humdjunx     242   29.5  c--cacc-c--------c-gc
   humdjunx     343   29.5  -cca-ca--------agc-ca
   musbjunx     607   29.5  --ct-a-ac--------cacc
   musdjunx     230   29.5  c-ctgcg-c--------gccc
   humcjunx     335   29.0  ---------tgcg--c-c-g-
```

FIG. 6



```
PROBE:      C: \HITACHI\JUNMIX.PRP
HYBRIDIZATION: C: \HITACHI\HUMBJU
Length = 374  Hairpin = 3  5
Locus     Pos  Tm
humbjunx 374  61.47  -------------
musbjunx 365  61.47  -------------
humdjunx 41   34.82  t---------g-g-
humbjunx 182  31.12  a---------gtgg
humdjunx 602  31.12  c---------c-gg
PROBE:      C: \HITACHI\JUNMIX.PRP
HYBRIDIZATION: C: \HITACHI\HUMBJU
Length = 467  Hairpin = 2  13
Locus     Pos  Tm
humbjunx 467  61.7   -------------
musbjunx 458  51.6   -----------c-
humdjunx 32   29.35  tgagcgg------
humdjunx 32   29.35  tgagcgg------
```

FIG. 6A (1)

```
PROBE: C:\HITACHI\JUNMIX.PRP
HYBRIDIZATION: C:\HITACHI\HUMBJUNX.CDS
Length = 374 Hairpin = 3 5
Locus     Pos Tm
humbjunx 374 61.47 -----------------
musbjunx 365 61.47 -----------------
humdjunx 41  34.82 t--------g-g--agt
humbjunx 182 31.12 a--------gtgg--gc
humdjunx 602 31.12 c--------c-ggg-gc
humdjunx 602 31.12 c--------c-ggg-gc

PROBE: C:\HITACHI\JUNMIX.PRP
HYBRIDIZATION: C:\HITACHI\HUMBJUNX.CDS
Length = 377 Hairpin = 2 14
Locus     Pos Tm
humbjunx 377 61.55 ------------------
musbjunx 368 61.55 ------------------
humdjunx 383 28.12 tg-cg-c--g--------
musdjunx 383 28.12 tg-ca-c--g--------
musdjunx 383 28.12 tg-ca-c--g--------

PROBE: C:\HITACHI\JUNMIX.PRP
HYBRIDIZATION: C:\HITACHI\HUMBJUNX.CDS
Length = 389 Hairpin = 3 3
Locus     Pos Tm
humbjunx 389 61.7  --------------------
muscjunx 314 56.65 -c------------------
musbjunx 380 50.85 ----------------t--g
humcjunx 314 49.35 -t-----------g------
humdjunx 395 33.85 -----------tt-gc--ag
musdjunx 395 33.85 -----------tt-gc--aa
humcjunx 326 32.35 g-ttcgcc----------tg
humdjunx 404 32.35 --ttcgcc----------t-
muscjunx 326 32.35 gcttcgcc----------tg
musdjunx 253 30.85 gacg-gct-ct---------
humbjunx 953 30.65 g--------t--c-cagct-
musdjunx 83  27.3  cc-gcggt-gt--------g
```

FIG. 6A (2)

```
PROBE: C:\HITACHI\JUNMIX.PRP
HYBRIDIZATION: C:\HITACHI\HUMBJUNX.CDS
Length = 397 Hairpin = 4 1
Locus     Pos Tm
humbjunx 397 61.55 ------------------
muscjunx 322 53.44 --------------g---
humcjunx 322 45.33 -----g--------g---
musbjunx 388 41.38 --------t--g-----t
humdjunx 214 36.83 ccccctgc----------
humdjunx 99  36.16 cg----gc-c--------
musdjunx 261 34.55 -ct----------gatct
humdjunx 400 33.27 c---ag--------g---
musdjunx 400 33.27 c---ag--------a---
humcjunx 334 32.28 ----------tgcg--c-
humdjunx 412 32.28 ----------t-a-g-c-
muscjunx 334 32.28 ----------tgcg--c-
humbjunx 658 30.17 cc-cc--------gt---
humdjunx 241 28.95 -c--cacc-c--------
humdjunx 342 28.95 c-cca-ca--------ag
musbjunx 606 28.95 ---ct-a-ac--------
musdjunx 229 28.95 -c-ctgcg-c--------
musdjunx 91  26.67 -gt--------gcc-ccg

PROBE: C:\HITACHI\JUNMIX.PRP
HYBRIDIZATION: C:\HITACHI\HUMBJUNX.CDS
Length = 417 Hairpin = 2 15
Locus     Pos Tm
humbjunx 417 60.08 -----------------------
musbjunx 408 55.52 ------------------c----
humdjunx 420 37.3  c-----g--------g---t-a-
musbjunx 61  29.0  g---gg--------ca-cctgt-
muscjunx 672 26.27 gc-gc--------a-g--aga--
```

FIG. 6A (3)

```
PROBE: C:\HITACHI\JUNMIX.PRP
HYBRIDIZATION: C:\HITACHI\HUMBJUNX.CDS
Length = 461 Hairpin = 4 9
Locus     Pos Tm
humbjunx 461 61.63 -------------------
musbjunx 452 61.63 -------------------
musbjunx 452 61.63 -------------------

PROBE: C:\HITACHI\JUNMIX.PRP
HYBRIDIZATION: C:\HITACHI\HUMBJUNX.CDS
Length = 467 Hairpin = 2 13
Locus     Pos Tm
humbjunx 467 61.7  --------------------
musbjunx 458 51.6  ----------------c-g-
humdjunx 32  29.35 tgagcgg--------gcgg-
humdjunx 32  29.35 tgagcgg--------gcgg-

PROBE: C:\HITACHI\JUNMIX.PRP
HYBRIDIZATION: C:\HITACHI\HUMBJUNX.CDS
Length = 477 Hairpin = 2 4
Locus     Pos Tm
humbjunx 477 61.37 ----------------
humdjunx 489 34.93 c-c---cg--------
humdjunx 489 34.93 c-c---cg--------

PROBE: C:\HITACHI\JUNMIX.PRP
HYBRIDIZATION: C:\HITACHI\HUMBJUNX.CDS
Length = 487 Hairpin = 3 3
Locus     Pos Tm
humbjunx 487 61.14 --------------
musdjunx 74  51.0  ct------------
humdjunx 499 45.64 ---------t---g
humdjunx 527 30.72 cc-c-c--------
musdjunx 97  30.72 ttc-c--------g
musdjunx 580 30.72 -cc--------t-g
musdjunx 637 30.72 cc-cc--------g
musdjunx 637 30.72 cc-cc--------g
```

FIG. 6A (4)

```
PROBE: C:\HITACHI\JUNMIX.PRP
HYBRIDIZATION: C:\HITACHI\HUMBJUNX.CDS
Length = 498 Hairpin = 3 2
Locus    Pos Tm
humbjunx 498 61.26 ---------------
humbjunx 498 61.26 ---------------

PROBE: C:\HITACHI\JUNMIX.PRP
HYBRIDIZATION: C:\HITACHI\HUMBJUNX.CDS
Length = 504 Hairpin = 3 2
Locus    Pos Tm
humbjunx 504 61.47 -----------------
musbjunx 495 40.35 c--a-----------t-
humdjunx 609 35.29 cg---------cgggg-
humdjunx 609 35.29 cg---------cgggg-
```

FIG. 7

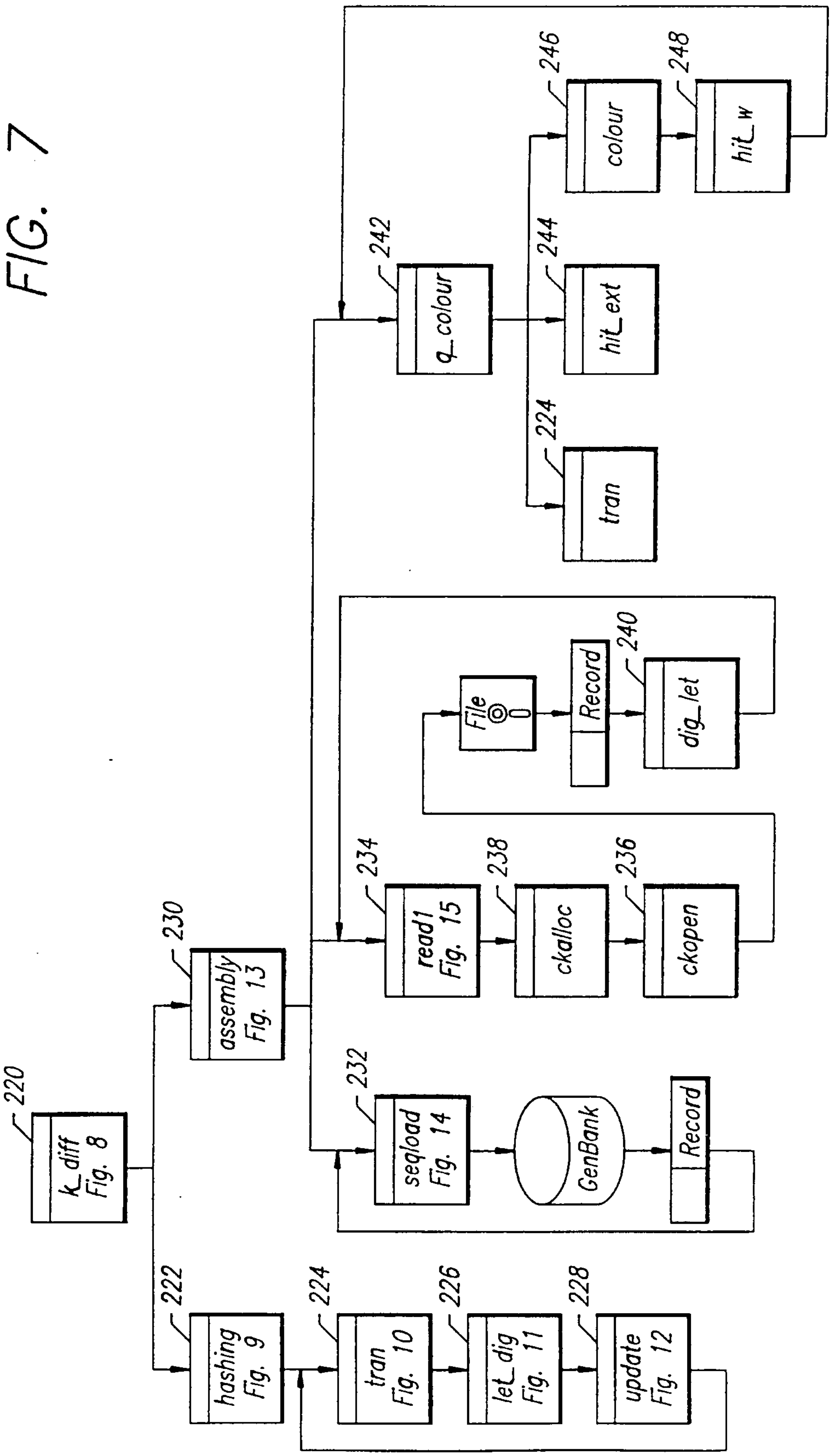

220
k_diff
Fig. 8
222
hashing
Fig. 9
224
tran
Fig. 10
226
let_dig
Fig. 11
228
update
Fig. 12
230
assembly
Fig. 13
232
seqload
Fig. 14
GenBank
Record
234
read1
Fig. 15
238
ckalloc
236
ckopen
File
Record
240
dig_let
242
q_colour
224
tran
244
hit_ext
246
colour
248
hit_w

FIG. 8(1)

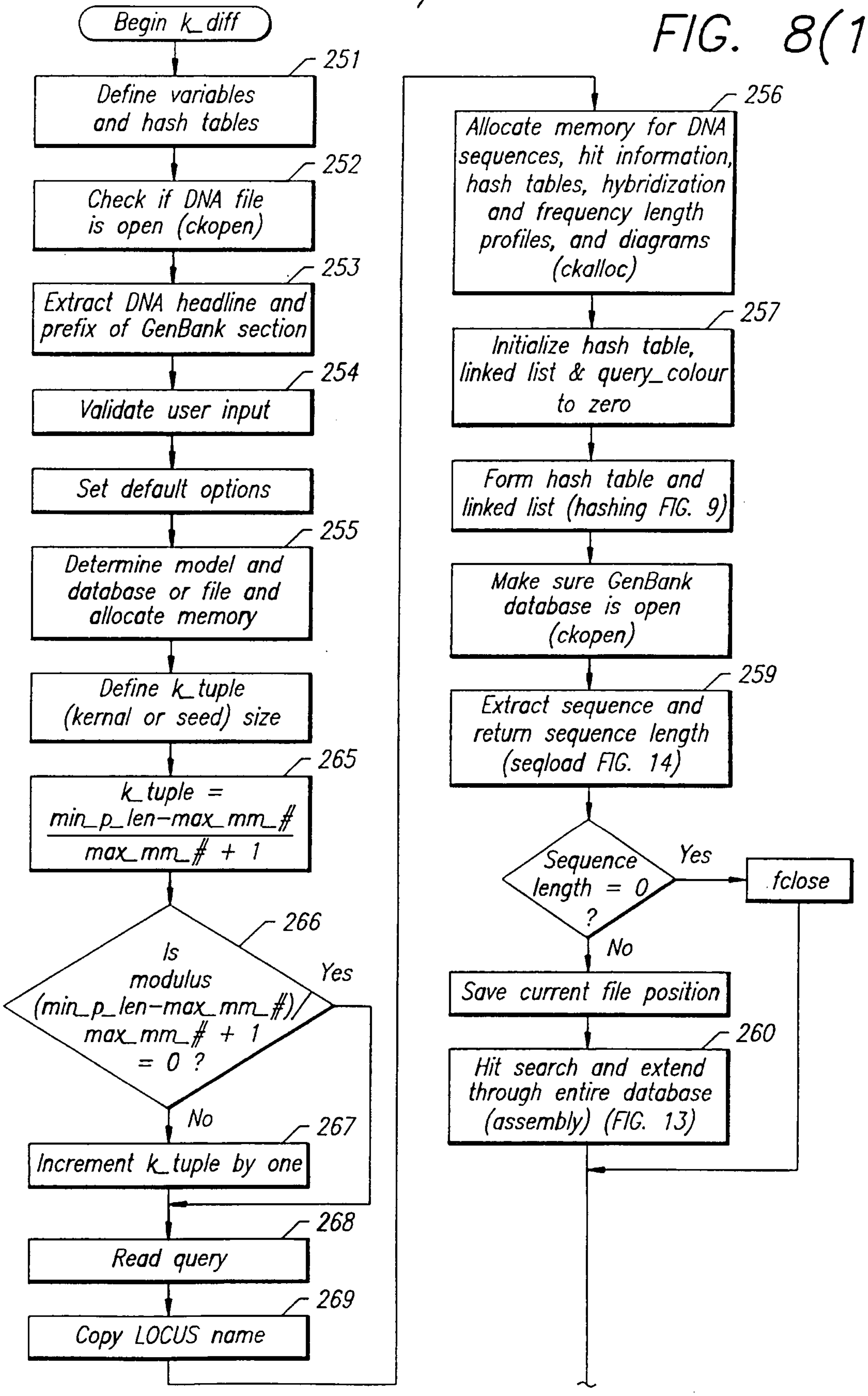

Begin k_diff
251
Define variables and hash tables
252
Check if DNA file is open (ckopen)
253
Extract DNA headline and prefix of GenBank section
254
Validate user input
Set default options
255
Determine model and database or file and allocate memory
Define k_tuple (kernal or seed) size
265
k_tuple = min_p_len−max_mm_# / max_mm_# + 1
266
Is modulus (min_p_len−max_mm_#)/ max_mm_# + 1 = 0 ?
Yes
No
267
Increment k_tuple by one
268
Read query
269
Copy LOCUS name
256
Allocate memory for DNA sequences, hit information, hash tables, hybridization and frequency length profiles, and diagrams (ckalloc)
257
Initialize hash table, linked list &amp; query_colour to zero
Form hash table and linked list (hashing FIG. 9)
Make sure GenBank database is open (ckopen)
259
Extract sequence and return sequence length (seqload FIG. 14)
Sequence length = 0 ?
Yes
fclose
No
Save current file position
260
Hit search and extend through entire database (assembly) (FIG. 13)

FIG. 8(2)

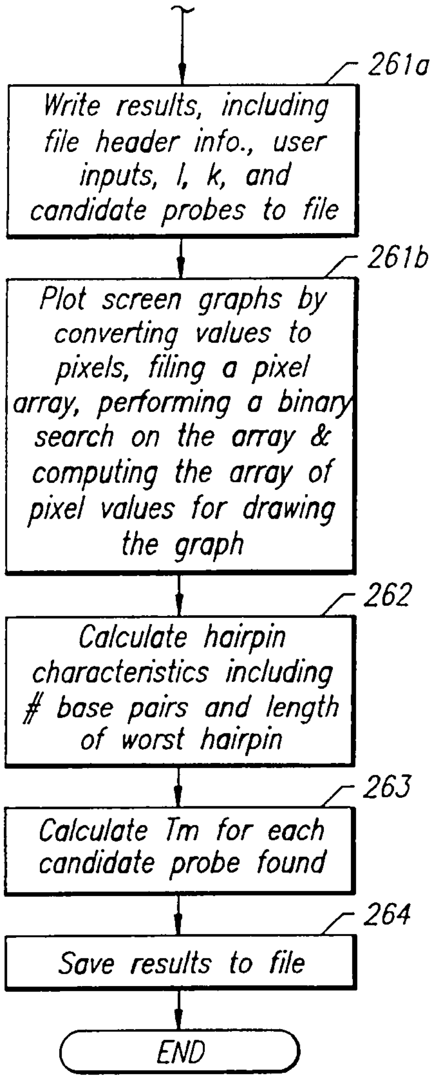

261a
Write results, including file header info., user inputs, l, k, and candidate probes to file
261b
Plot screen graphs by converting values to pixels, filing a pixel array, performing a binary search on the array & computing the array of pixel values for drawing the graph
262
Calculate hairpin characteristics including # base pairs and length of worst hairpin
263
Calculate Tm for each candidate probe found
264
Save results to file
END

FIG. 9

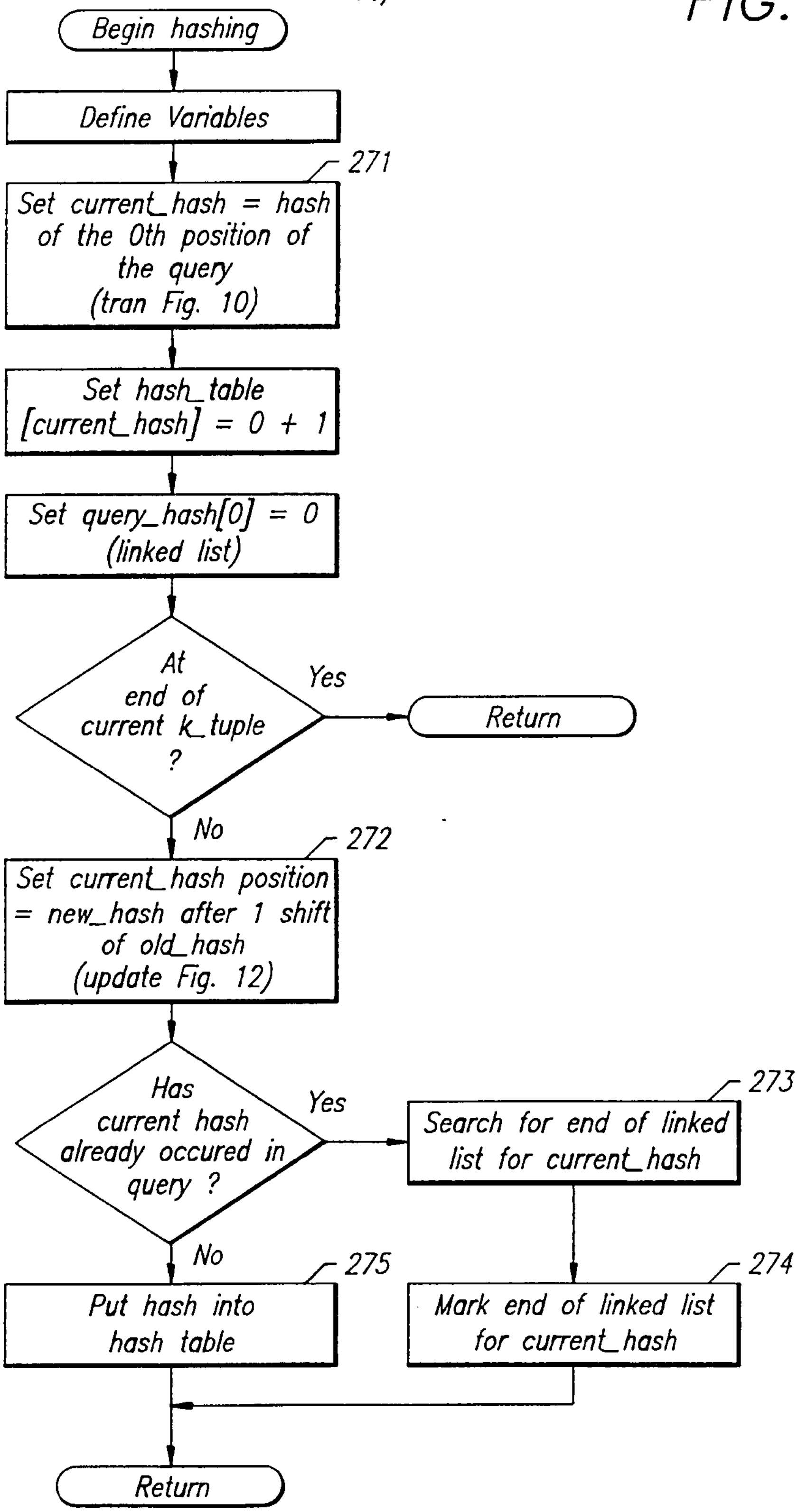

Begin hashing
Define Variables
271
Set current_hash = hash of the 0th position of the query (tran Fig. 10)
Set hash_table [current_hash] = 0 + 1
Set query_hash[0] = 0 (linked list)
At end of current k_tuple ?
Yes
Return
No
272
Set current_hash position = new_hash after 1 shift of old_hash (update Fig. 12)
Has current hash already occured in query ?
Yes
273
Search for end of linked list for current_hash
No
275
Put hash into hash table
274
Mark end of linked list for current_hash
Return

FIG. 10

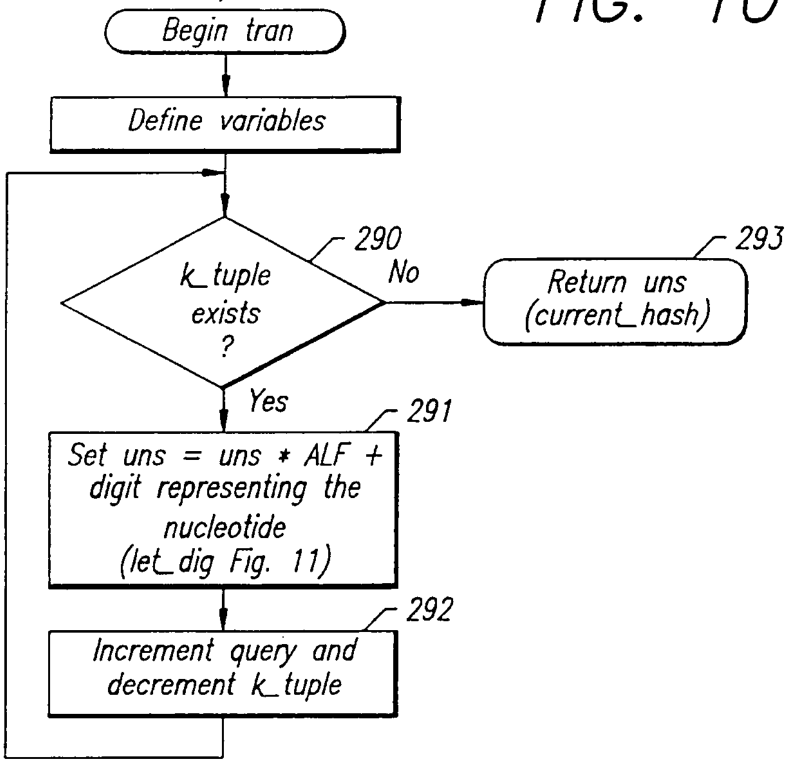

Begin tran
Define variables
k_tuple exists ?
290
No
Return uns (current_hash)
293
Yes
Set uns = uns * ALF + digit representing the nucleotide (let_dig Fig. 11)
291
Increment query and decrement k_tuple
292

FIG. 12

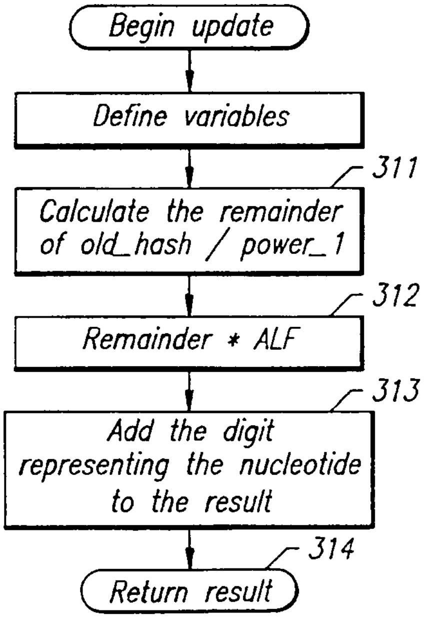

Begin update
Define variables
Calculate the remainder of old_hash / power_1
311
Remainder * ALF
312
Add the digit representing the nucleotide to the result
313
Return result
314

FIG. 11

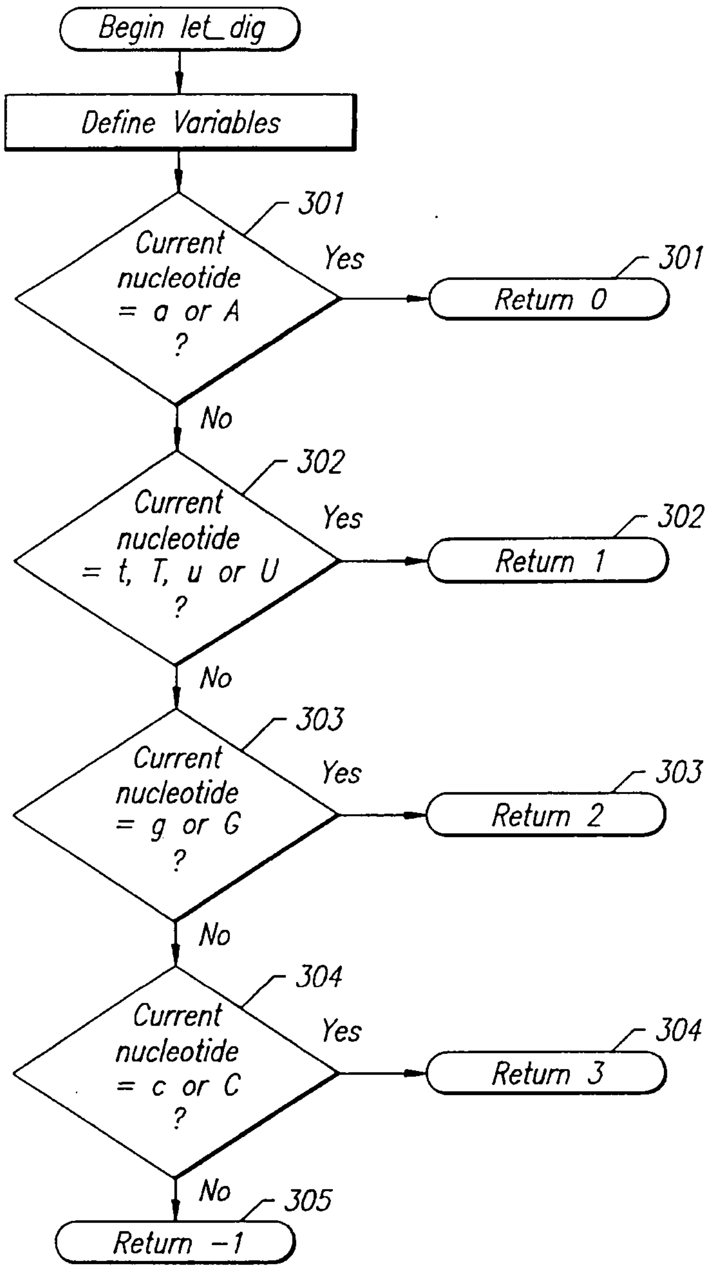
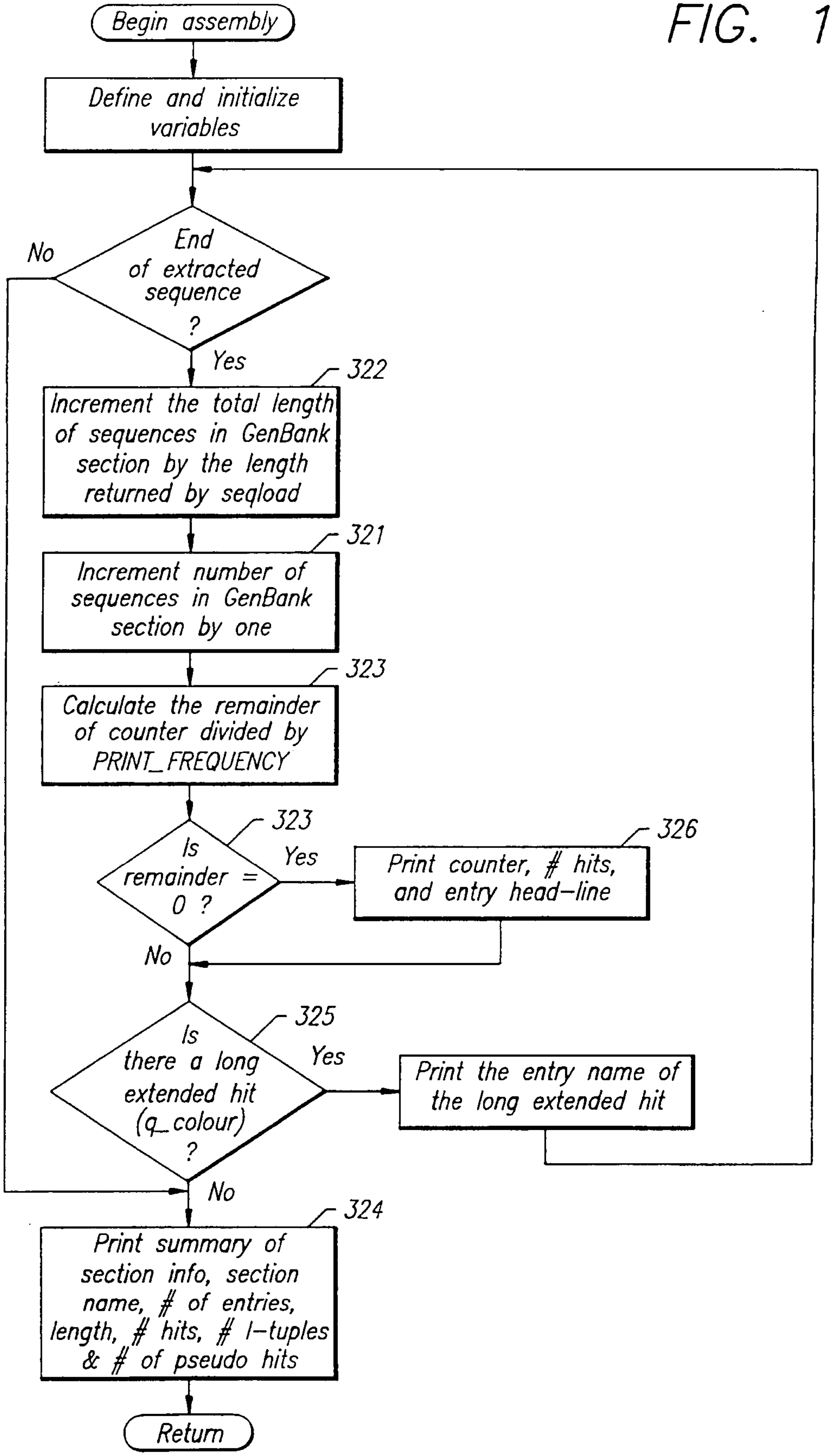

Begin let_dig
Define Variables
301
Current nucleotide = a or A ?
Yes
301
Return 0
No
302
Current nucleotide = t, T, u or U ?
Yes
302
Return 1
No
303
Current nucleotide = g or G ?
Yes
303
Return 2
No
304
Current nucleotide = c or C ?
Yes
304
Return 3
No
305
Return −1

FIG. 13


Begin assembly
Define and initialize variables
End of extracted sequence ?
No
Yes
322
Increment the total length of sequences in GenBank section by the length returned by seqload
321
Increment number of sequences in GenBank section by one
323
Calculate the remainder of counter divided by PRINT_FREQUENCY
323
Is remainder = 0 ?
Yes
326
Print counter, # hits, and entry head-line
No
325
Is there a long extended hit (q_colour) ?
Yes
Print the entry name of the long extended hit
No
324
Print summary of section info, section name, # of entries, length, # hits, # l-tuples & # of pseudo hits
Return

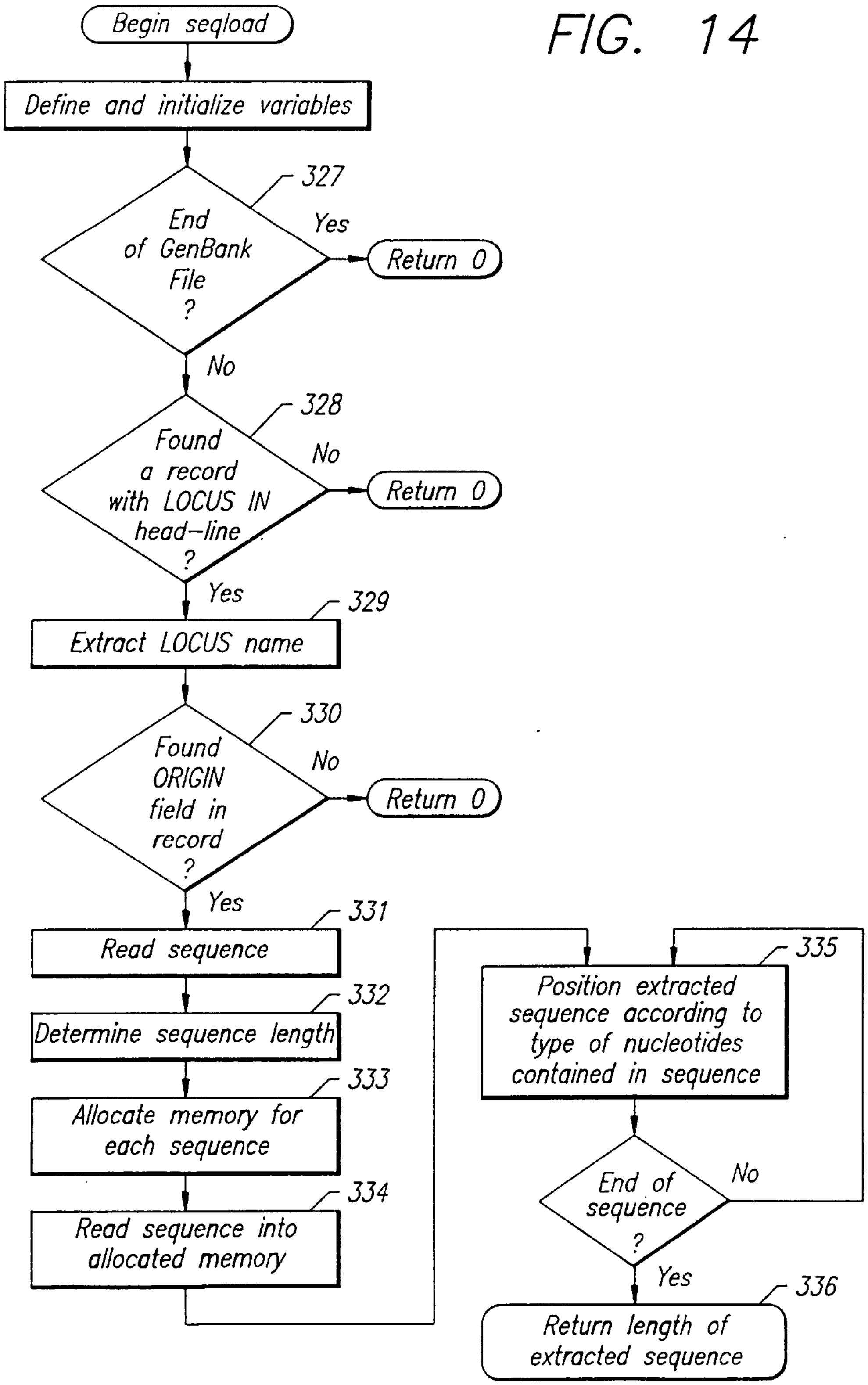

Begin seqload
Define and initialize variables
327
End of GenBank File ?
Yes
Return 0
No
328
Found a record with LOCUS IN head–line ?
No
Return 0
Yes
329
Extract LOCUS name
330
Found ORIGIN field in record ?
No
Return 0
Yes
331
Read sequence
332
Determine sequence length
333
Allocate memory for each sequence
334
Read sequence into allocated memory
335
Position extracted sequence according to type of nucleotides contained in sequence
End of sequence ?
No
Yes
336
Return length of extracted sequence

FIG. 14

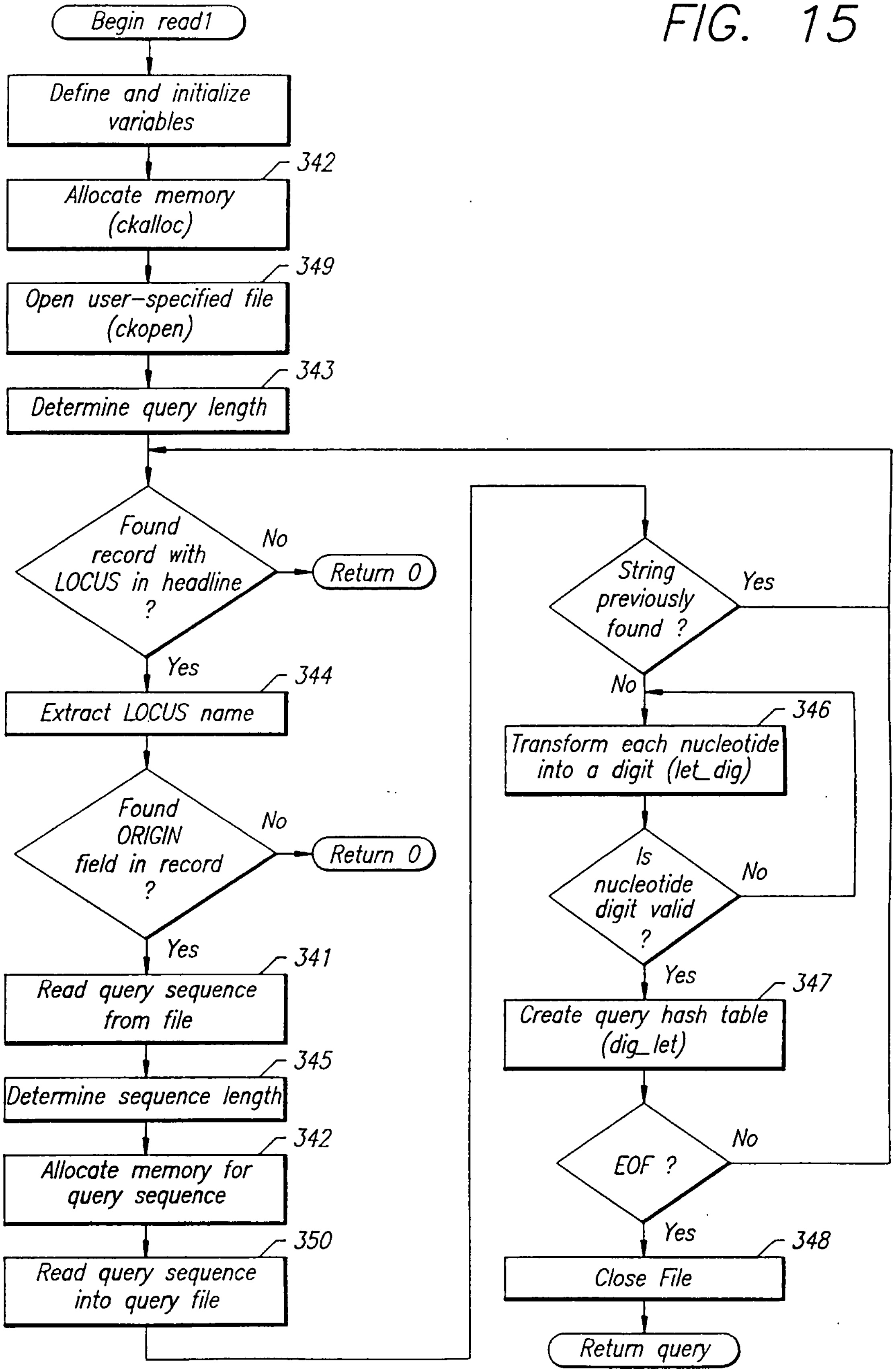

Begin read1
Define and initialize variables
342
Allocate memory (ckalloc)
349
Open user-specified file (ckopen)
343
Determine query length
Found record with LOCUS in headline ?
No
Return 0
Yes
344
Extract LOCUS name
Found ORIGIN field in record ?
No
Return 0
Yes
341
Read query sequence from file
345
Determine sequence length
342
Allocate memory for query sequence
350
Read query sequence into query file
String previously found ?
Yes
No
346
Transform each nucleotide into a digit (let_dig)
Is nucleotide digit valid ?
No
Yes
347
Create query hash table (dig_let)
EOF ?
No
Yes
348
Close File
Return query

FIG. 15

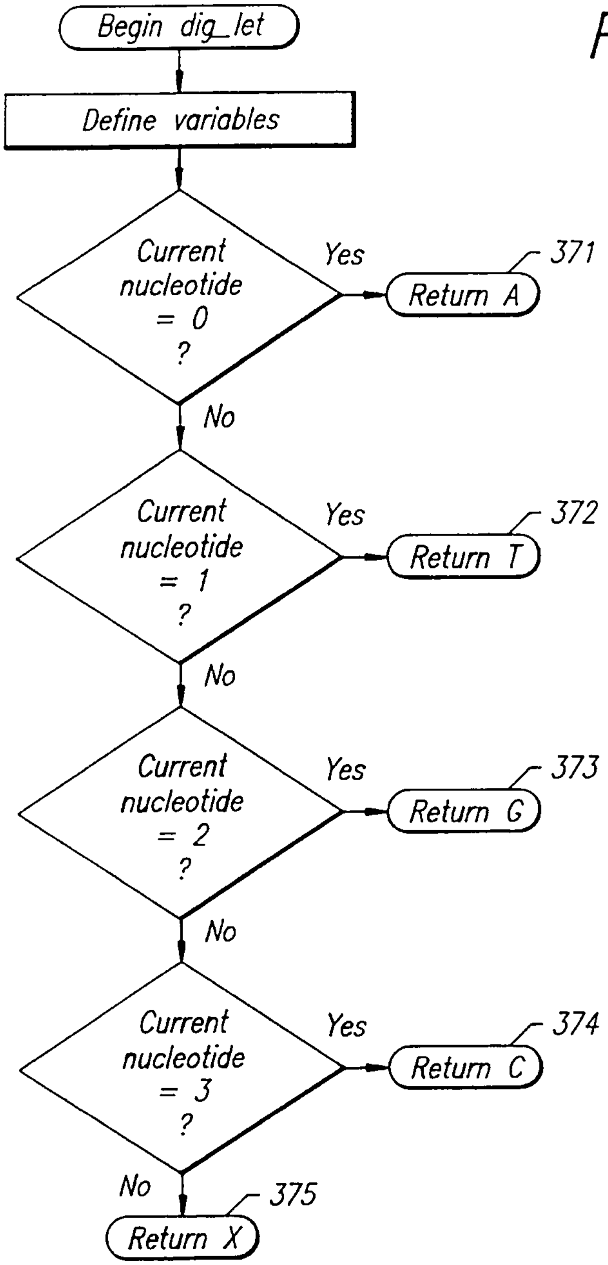
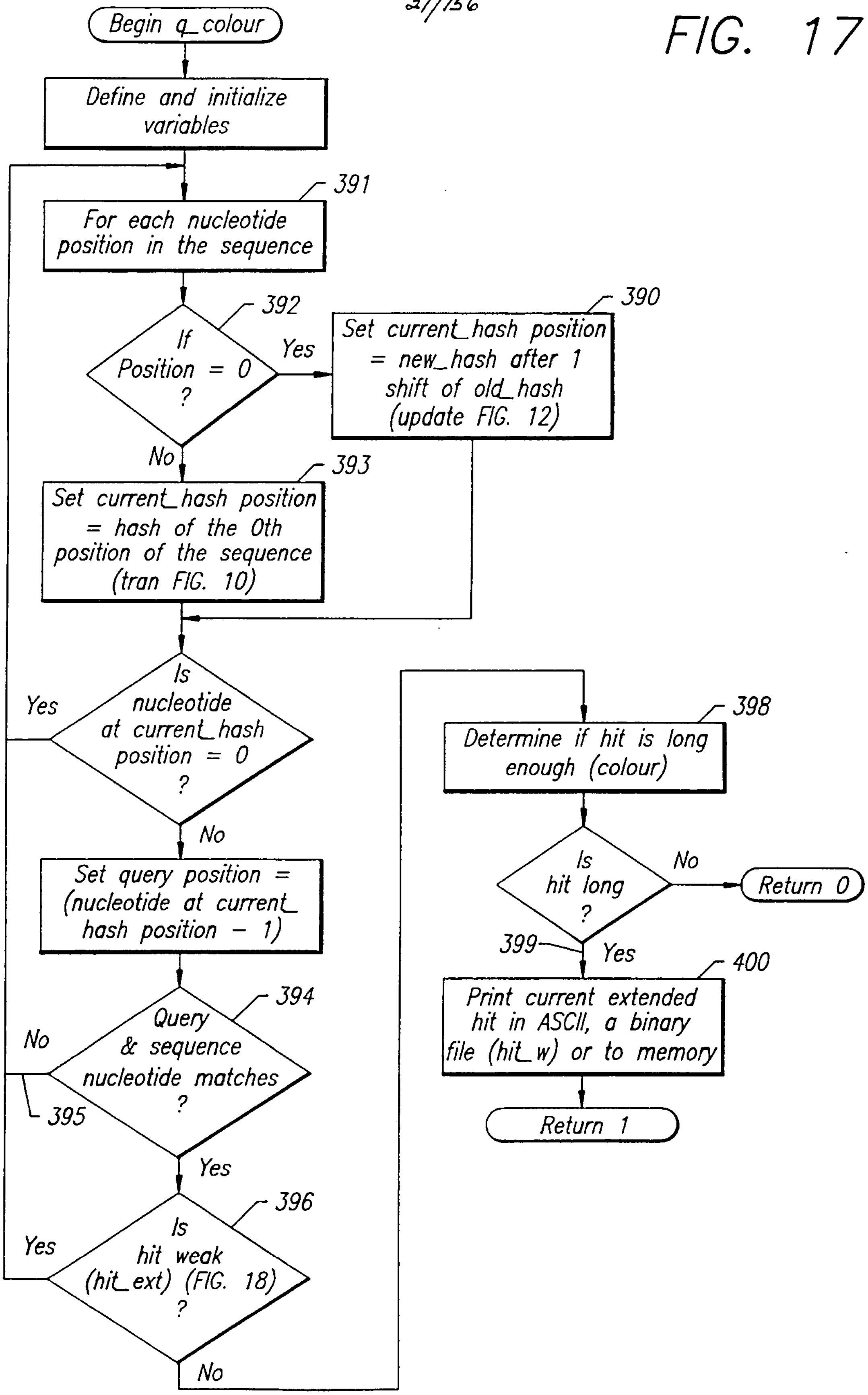

Begin dig_let
Define variables
Current nucleotide = 0 ?
Yes
Return A
371
No
Current nucleotide = 1 ?
Yes
Return T
372
No
Current nucleotide = 2 ?
Yes
Return G
373
No
Current nucleotide = 3 ?
Yes
Return C
374
No
Return X
375

FIG. 16

FIG. 17


Begin q_colour
Define and initialize variables
391
For each nucleotide position in the sequence
392
If Position = 0 ?
Yes
No
390
Set current_hash position = new_hash after 1 shift of old_hash (update FIG. 12)
393
Set current_hash position = hash of the 0th position of the sequence (tran FIG. 10)
Yes
Is nucleotide at current_hash position = 0 ?
No
Set query position = (nucleotide at current_hash position − 1)
394
No
Query & sequence nucleotide matches ?
395
Yes
396
Yes
Is hit weak (hit_ext) (FIG. 18) ?
No
398
Determine if hit is long enough (colour)
Is hit long ?
No
Return 0
399
Yes
400
Print current extended hit in ASCII, a binary file (hit_w) or to memory
Return 1

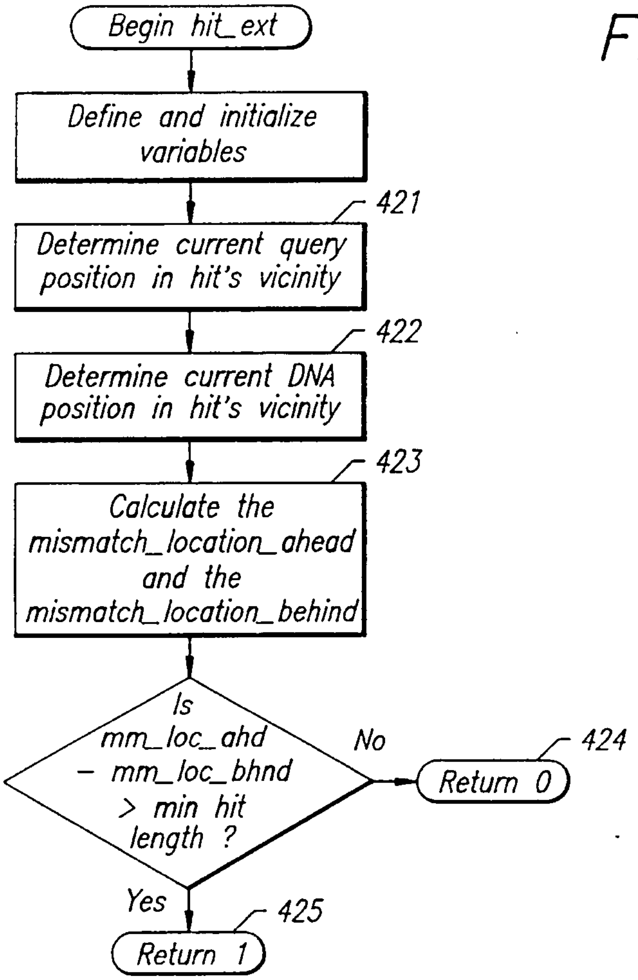

Begin hit_ext
Define and initialize variables
421
Determine current query position in hit's vicinity
422
Determine current DNA position in hit's vicinity
423
Calculate the mismatch_location_ahead and the mismatch_location_behind
Is mm_loc_ahd – mm_loc_bhnd > min hit length ?
No
424
Return 0
Yes
425
Return 1

FIG. 18

FIG. 19

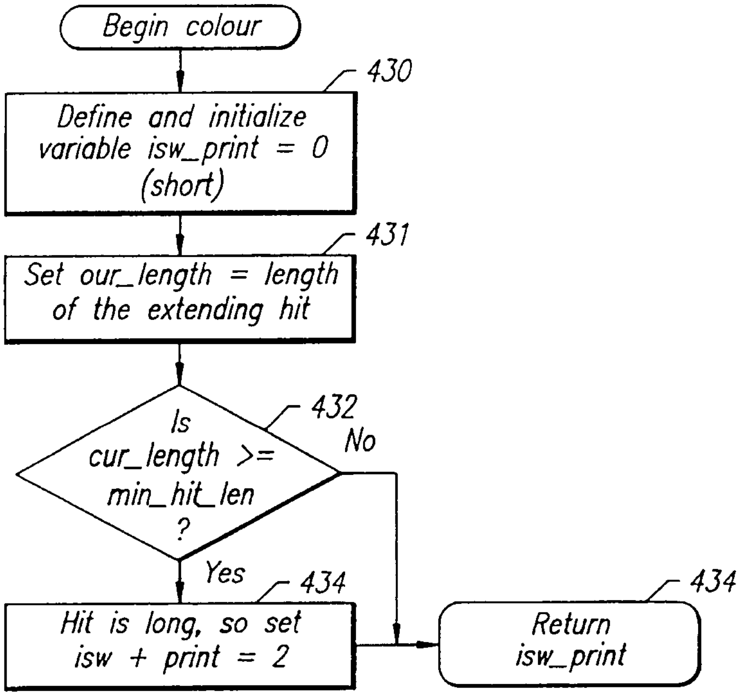

Begin colour
430
Define and initialize variable isw_print = 0 (short)
431
Set our_length = length of the extending hit
432
Is cur_length >= min_hit_len ?
No
Yes
434
Hit is long, so set isw + print = 2
434
Return isw_print

FIG. 20 (1)

```
OligoProbe DesignStation

Probes:   C:\HITACHI\HUMBJUNX.CDS
Datatbase:   C:\HITACHI\JUNMIX.SEQ

Mismatch Model, l = 21, k = 4

 Position     Mismatches                                   screensN
   length     0     1     2     3     4     5     6     7     8        Probe

     1 21     1     1     1     1     1  ATGTGCACTAAAATGGAACAG
     2 21     1     1     1     1     1  TGTGCACTAAAATGGAACAGC
     3 21     1     1     1     1     1  GTGCACTAAAATGGAACAGCC
     4 21     1     1     1     1     1  TGCACTAAAATGGAACAGCCC
     5 21     1     1     1     1     1  GCACTAAAATGGAACAGCCCT
     6 21     1     1     1     1     1  CACTAAAATGGAACAGCCCTT
     7 21     1     1     1     1     1  ACTAAAATGGAACAGCCCTTC
     8 21     1     1     1     1     1  CTAAAATGGAACAGCCCTTCT
     9 21     1     1     1     1     1  TAAAATGGAACAGCCCTTCTA
    10 21     1     1     1     1     1  AAAATGGAACAGCCCTTCTAC
    11 21     1     1     1     1     1  AAATGGAACAGCCCTTCTACC
    12 21     1     1     1     1     1  AATGGAACAGCCCTTCTACCA
    13 21     1     1     1     1     1  ATGGAACAGCCCTTCTACCAC
    14 21     1     1     1     1     1  TGGAACAGCCCTTCTACCACG
```

FIG. 20 (2)

15	21	1	1	1	1	1	GGAACAGCCCTTCTACCACGA
16	21	1	1	1	1	1	GAACAGCCCTTCTACCACGAC
17	21	1	1	1	1	1	AACAGCCCTTCTACCACGACG
18	21	1	1	1	1	1	ACAGCCCTTCTACCACGACGA
19	21	1	1	1	1	1	CAGCCCTTCTACCACGACGAC
20	21	1	1	1	1	1	AGCCCTTCTACCACGACGACT
21	21	1	1	1	1	1	GCCCTTCTACCACGACGACTC
22	21	1	1	1	1	1	CCCTTCTACCACGACGACTCA
23	21	1	1	1	1	1	CCTTCTACCACGACGACTCAT
24	21	1	1	1	1	1	CTTCTACCACGACGACTCATA
25	21	1	1	1	1	1	TTCTACCACGACGACTCATAC
26	21	1	1	1	1	1	TCTACCACGACGACTCATACA
27	21	1	1	1	1	1	CTACCACGACGACTCATACAC
28	21	1	1	1	1	1	TACCACGACGACTCATACACA
29	21	1	1	1	1	1	ACCACGACGACTCATACACAG
30	21	1	1	1	1	1	CCACGACGACTCATACACAGC
31	21	1	1	1	1	1	CACGACGACTCATACACAGCT
32	21	1	1	1	1	1	ACGACGACTCATACACAGCTA
33	21	1	1	1	1	1	CGACGACTCATACACAGCTAC
34	21	1	1	1	1	1	GACGACTCATACACAGCTACG
35	21	1	1	1	1	1	ACGACTCATACACAGCTACGG
36	21	1	1	1	1	1	CGACTCATACACAGCTACGGG

FIG. 20 (3)

37	21	1	1	1	1	1	GACTCATACACAGCTACGGGA
38	21	1	1	1	1	1	ACTCATACACAGCTACGGGAT
39	21	1	1	1	1	1	CTCATACACAGCTACGGGATA
40	21	1	1	1	1	1	TCATACACAGCTACGGGATAC
41	21	1	1	1	1	1	CATACACAGCTACGGGATACG
42	21	1	1	1	1	1	ATACACAGCTACGGGATACGG
43	21	1	1	1	1	1	TACACAGCTACGGGATACGGC
44	21	1	1	1	1	1	ACACAGCTACGGGATACGGCC
45	21	1	1	1	1	1	CACAGCTACGGGATACGGCCG
46	21	1	1	1	1	1	ACAGCTACGGGATACGGCCGG
47	21	1	1	1	1	1	CAGCTACGGGATACGGCCGGG
48	21	1	1	1	1	1	AGCTACGGGATACGGCCGGGC
49	21	1	1	1	1	1	GCTACGGGATACGGCCGGGCC
50	21	1	1	1	1	1	CTACGGGATACGGCCGGGCCC
51	21	1	1	1	1	1	TACGGGATACGGCCGGGCCCC
52	21	1	1	1	1	1	ACGGGATACGGCCGGGCCCCT
53	21	1	1	1	1	1	CGGGATACGGCCGGGCCCCTG

FIG. 20 (4)

54	21	1	1	1	1	1	GGGATACGGCCGGGCCCCTGG
55	21	1	1	1	1	1	GGATACGGCCGGGCCCCTGGT
56	21	1	1	1	1	1	GATACGGCCGGGCCCCTGGTG
57	21	1	1	1	1	1	ATACGGCCGGGCCCCTGGTGG
58	21	1	1	1	1	1	TACGGCCGGGCCCCTGGTGGC
59	21	1	1	1	1	1	ACGGCCGGGCCCCTGGTGGCC
60	21	1	1	1	1	1	CGGCCGGGCCCCTGGTGGCCT
61	21	1	1	1	1	1	GGCCGGGCCCCTGGTGGCCTC
62	21	1	1	1	1	1	GCCGGGCCCCTGGTGGCCTCT
63	21	1	1	1	1	1	CCGGGCCCCTGGTGGCCTCTC
64	21	1	1	1	1	1	CGGGCCCCTGGTGGCCTCTCT
65	21	1	1	1	1	1	GGGCCCCTGGTGGCCTCTCTC
66	21	1	1	1	1	1	GGCCCCTGGTGGCCTCTCTCT
67	21	1	1	1	1	1	GCCCCTGGTGGCCTCTCTCTA
68	21	1	1	1	1	1	CCCCTGGTGGCCTCTCTCTAC
69	21	1	1	1	1	1	CCCTGGTGGCCTCTCTCTACA
70	21	1	1	1	1	1	CCTGGTGGCCTCTCTCTACAC
71	21	1	1	1	1	1	CTGGTGGCCTCTCTCTACACG
72	21	1	1	1	1	1	TGGTGGCCTCTCTCTACACGA
73	21	1	1	1	1	1	GGTGGCCTCTCTCTACACGAC
74	21	1	1	1	1	1	GTGGCCTCTCTCTACACGACT

FIG. 20 (5)

75	21	1	1	1	1	1	TGGCCTCTCTCTACACGACTA
76	21	1	1	1	1	1	GGCCTCTCTCTACACGACTAC
77	21	1	1	1	1	1	GCCTCTCTCTACACGACTACA
78	21	1	1	1	1	1	CCTCTCTCTACACGACTACAA
79	21	1	1	1	1	1	CTCTCTCTACACGACTACAAA
80	21	1	1	1	1	1	TCTCTCTACACGACTACAAAC
81	21	1	1	1	1	1	CTCTCTACACGACTACAAACT
82	21	1	1	1	1	1	TCTCTACACGACTACAAACTC
83	21	1	1	1	1	1	CTCTACACGACTACAAACTCC
84	21	1	1	1	1	1	TCTACACGACTACAAACTCCT
85	21	1	1	1	1	1	CTACACGACTACAAACTCCTG
86	21	1	1	1	1	1	TACACGACTACAAACTCCTGA
87	21	1	1	1	1	1	ACACGACTACAAACTCCTGAA
88	21	1	1	1	1	1	CACGACTACAAACTCCTGAAA
89	21	1	1	1	1	1	ACGACTACAAACTCCTGAAAC
90	21	1	1	1	1	1	CGACTACAAACTCCTGAAACC
91	21	1	1	1	1	1	GACTACAAACTCCTGAAACCG
92	21	1	1	1	1	1	ACTACAAACTCCTGAAACCGA
93	21	1	1	1	1	1	CTACAAACTCCTGAAACCGAG
94	21	1	1	1	1	1	TACAAACTCCTGAAACCGAGC
95	21	1	1	1	1	1	ACAAACTCCTGAAACCGAGCC

FIG. 20 (6)

96	21	1	1	1	1	1	CAAACTCCTGAAACCGAGCCT
97	21	1	1	1	1	1	AAACTCCTGAAACCGAGCCTG
98	21	1	1	1	1	1	AACTCCTGAAACCGAGCCTGG
99	21	1	1	1	1	1	ACTCCTGAAACCGAGCCTGGC
100	21	1	1	1	1	1	CTCCTGAAACCGAGCCTGGCG
101	21	1	1	1	1	1	TCCTGAAACCGAGCCTGGCGG
102	21	1	1	1	1	1	CCTGAAACCGAGCCTGGCGGT
103	21	1	1	1	1	1	CTGAAACCGAGCCTGGCGGTC
104	21	1	1	1	1	1	TGAAACCGAGCCTGGCGGTCA
105	21	1	1	1	1	1	GAAACCGAGCCTGGCGGTCAA
106	21	1	1	1	1	1	AAACCGAGCCTGGCGGTCAAC
107	21	1	1	1	1	1	AACCGAGCCTGGCGGTCAACC
108	21	1	1	1	1	1	ACCGAGCCTGGCGGTCAACCT
109	21	1	1	1	1	1	CCGAGCCTGGCGGTCAACCTG
110	21	1	1	1	1	1	CGAGCCTGGCGGTCAACCTGG
111	21	1	1	1	1	1	GAGCCTGGCGGTCAACCTGGC
112	21	1	1	1	1	1	AGCCTGGCGGTCAACCTGGCC
113	21	1	1	1	1	1	GCCTGGCGGTCAACCTGGCCG
114	21	1	1	1	1	1	CCTGGCGGTCAACCTGGCCGA
115	21	1	1	1	1	1	CTGGCGGTCAACCTGGCCGAC
116	21	1	1	1	1	1	TGGCGGTCAACCTGGCCGACC

FIG. 20 (7)

117	21	1	1	1	1	1	GGCGGTCAACCTGGCCGACCC
118	21	1	1	1	1	1	GCGGTCAACCTGGCCGACCCC
119	21	1	1	1	1	1	CGGTCAACCTGGCCGACCCCT
120	21	1	1	1	1	1	GGTCAACCTGGCCGACCCCTA
121	21	1	1	1	1	1	GTCAACCTGGCCGACCCCTAC
122	21	1	1	1	1	1	TCAACCTGGCCGACCCCTACC
123	21	1	1	1	1	1	CAACCTGGCCGACCCCTACCG
124	21	1	1	1	1	1	AACCTGGCCGACCCCTACCGG
125	21	1	1	1	1	1	ACCTGGCCGACCCCTACCGGA
126	21	1	1	1	1	1	CCTGGCCGACCCCTACCGGAG
127	21	1	1	1	1	1	CTGGCCGACCCCTACCGGAGT
128	21	1	1	1	1	1	TGGCCGACCCCTACCGGAGTC
129	21	1	1	1	1	1	GGCCGACCCCTACCGGAGTCT
130	21	1	1	1	1	1	GCCGACCCCTACCGGAGTCTC
131	21	1	1	1	1	1	CCGACCCCTACCGGAGTCTCA
132	21	1	1	1	1	1	CGACCCCTACCGGAGTCTCAA
133	21	1	1	1	1	1	GACCCCTACCGGAGTCTCAAA
134	21	1	1	1	1	1	ACCCCTACCGGAGTCTCAAAG
135	21	1	1	1	1	1	CCCCTACCGGAGTCTCAAAGC
136	21	1	1	1	1	1	CCCTACCGGAGTCTCAAAGCG
137	21	1	1	1	1	1	CCTACCGGAGTCTCAAAGCGC

FIG. 20 (8)

138	21	1	1	1	1	1	CTACCGGAGTCTCAAAGCGCC
139	21	1	1	1	1	1	TACCGGAGTCTCAAAGCGCCT
140	21	1	1	1	1	1	ACCGGAGTCTCAAAGCGCCTG
141	21	1	1	1	1	1	CCGGAGTCTCAAAGCGCCTGG
142	21	1	1	1	1	1	CGGAGTCTCAAAGCGCCTGGG
143	21	1	1	1	1	1	GGAGTCTCAAAGCGCCTGGGG
144	21	1	1	1	1	1	GAGTCTCAAAGCGCCTGGGGC
145	21	1	1	1	1	1	AGTCTCAAAGCGCCTGGGGCT
146	21	1	1	1	1	1	GTCTCAAAGCGCCTGGGGCTC
147	21	1	1	1	1	1	TCTCAAAGCGCCTGGGGCTCG
148	21	1	1	1	1	1	CTCAAAGCGCCTGGGGCTCGC
149	21	1	1	1	1	1	TCAAAGCGCCTGGGGCTCGCG
150	21	1	1	1	1	1	CAAAGCGCCTGGGGCTCGCGG
151	21	1	1	1	1	1	AAAGCGCCTGGGGCTCGCGGA
152	21	1	1	1	1	1	AAGCGCCTGGGGCTCGCGGAC
153	21	1	1	1	1	1	AGCGCCTGGGGCTCGCGGACC
154	21	1	1	1	1	1	GCGCCTGGGGCTCGCGGACCC
155	21	1	1	1	1	1	CGCCTGGGGCTCGCGGACCCG
156	21	1	1	1	1	1	GCCTGGGGCTCGCGGACCCGG
157	21	1	1	1	1	1	CCTGGGGCTCGCGGACCCGGC
158	21	1	1	1	1	1	CTGGGGCTCGCGGACCCGGCC

FIG. 20 (9)

159	21	1	1	1	1	1	TGGGGCTCGCGGACCCGGCCC
160	21	1	1	1	1	1	GGGGCTCGCGGACCCGGCCCA
161	21	1	1	1	1	1	GGGCTCGCGGACCCGGCCCAG
162	21	1	1	1	1	1	GGCTCGCGGACCCGGCCCAGA
163	21	1	1	1	1	1	GCTCGCGGACCCGGCCCAGAG
164	21	1	1	1	1	1	CTCGCGGACCCGGCCCAGAGG
165	21	1	1	1	1	1	TCGCGGACCCGGCCCAGAGGG
166	21	1	1	1	1	1	CGCGGACCCGGCCCAGAGGGC
167	21	1	1	1	1	1	GCGGACCCGGCCCAGAGGGCG
168	21	1	1	1	1	1	CGGACCCGGCCCAGAGGGCGG
169	21	1	1	1	1	1	GGACCCGGCCCAGAGGGCGGC
170	21	1	1	1	1	1	GACCCGGCCCAGAGGGCGGCG
171	21	1	1	1	1	1	ACCCGGCCCAGAGGGCGGCGG
172	21	1	1	1	1	1	CCCGGCCCAGAGGGCGGCGGT
173	21	1	1	1	1	1	CCGGCCCAGAGGGCGGCGGTG
174	21	1	1	1	1	1	CGGCCCAGAGGGCGGCGGTGG
175	21	1	1	1	1	1	GGCCCAGAGGGCGGCGGTGGC
176	21	1	1	1	1	1	GCCCAGAGGGCGGCGGTGGCG
177	21	1	1	1	1	1	CCCAGAGGGCGGCGGTGGCGG
178	21	1	1	1	1	1	CCAGAGGGCGGCGGTGGCGGC
179	21	1	1	1	1	1	CAGAGGGCGGCGGTGGCGGCA
180	21	1	1	1	1	1	AGAGGGCGGCGGTGGCGGCAG

FIG. 20 (10)

181	21	1	1	1	1	1	GAGGGCGGCGGTGGCGGCAGC
182	21	1	1	1	1	1	AGGGCGGCGGTGGCGGCAGCT
183	21	1	1	1	1	1	GGGCGGCGGTGGCGGCAGCTA
184	21	1	1	1	1	1	GGCGGCGGTGGCGGCAGCTAC
185	21	1	1	1	1	1	GCGGCGGTGGCGGCAGCTACT
186	21	1	1	1	1	1	CGGCGGTGGCGGCAGCTACTT
187	21	1	1	1	1	1	GGCGGTGGCGGCAGCTACTTT
188	21	1	1	1	1	1	GCGGTGGCGGCAGCTACTTTT
189	21	1	1	1	1	1	CGGTGGCGGCAGCTACTTTTC
190	21	1	1	1	1	1	GGTGGCGGCAGCTACTTTTCT
191	21	1	1	1	1	1	GTGGCGGCAGCTACTTTTCTG
192	21	1	1	1	1	1	TGGCGGCAGCTACTTTTCTGG
193	21	1	1	1	1	1	GGCGGCAGCTACTTTTCTGGT
194	21	1	1	1	1	1	GCGGCAGCTACTTTTCTGGTC
195	21	1	1	1	1	1	CGGCAGCTACTTTTCTGGTCA
196	21	1	1	1	1	1	GGCAGCTACTTTTCTGGTCAG
197	21	1	1	1	1	1	GCAGCTACTTTTCTGGTCAGG
198	21	1	1	1	1	1	CAGCTACTTTTCTGGTCAGGG
199	21	1	1	1	1	1	AGCTACTTTTCTGGTCAGGGC
200	21	1	1	1	1	1	GCTACTTTTCTGGTCAGGGCT
201	21	1	1	1	1	1	CTACTTTTCTGGTCAGGGCTC

FIG. 20 (11)

202	21	1	1	1	1	1	TACTTTTCTGGTCAGGGCTCG
203	21	1	1	1	1	1	ACTTTTCTGGTCAGGGCTCGG
204	21	1	1	1	1	1	CTTTTCTGGTCAGGGCTCGGA
205	21	1	1	1	1	1	TTTTCTGGTCAGGGCTCGGAC
206	21	1	1	1	1	1	TTTCTGGTCAGGGCTCGGACA
207	21	1	1	1	1	1	TTCTGGTCAGGGCTCGGACAC
208	21	1	1	1	1	1	TCTGGTCAGGGCTCGGACACC
209	21	1	1	1	1	1	CTGGTCAGGGCTCGGACACCG
210	21	1	1	1	1	1	TGGTCAGGGCTCGGACACCGG
211	21	1	1	1	1	1	GGTCAGGGCTCGGACACCGGC
212	21	1	1	1	1	1	GTCAGGGCTCGGACACCGGCG
213	21	1	1	1	1	1	TCAGGGCTCGGACACCGGCGC
214	21	1	1	1	1	1	CAGGGCTCGGACACCGGCGCG
215	21	1	1	1	1	1	AGGGCTCGGACACCGGCGCGT
216	21	1	1	1	1	1	GGGCTCGGACACCGGCGCGTC
217	21	1	1	1	1	1	GGCTCGGACACCGGCGCGTCT
218	21	1	1	1	1	1	GCTCGGACACCGGCGCGTCTC
219	21	1	1	1	1	1	CTCGGACACCGGCGCGTCTCT
220	21	1	1	1	1	1	TCGGACACCGGCGCGTCTCTC
221	21	1	1	1	1	1	CGGACACCGGCGCGTCTCTCA
222	21	1	1	1	1	1	GGACACCGGCGCGTCTCTCAA

FIG. 20 (12)

223	21	1	1	1	1	1	GACACCGGCGCGTCTCTCAAG
224	21	1	1	1	1	1	ACACCGGCGCGTCTCTCAAGC
225	21	1	1	1	1	1	CACCGGCGCGTCTCTCAAGCT
226	21	1	1	1	1	1	ACCGGCGCGTCTCTCAAGCTC
227	21	1	1	1	1	1	CCGGCGCGTCTCTCAAGCTCG
228	21	1	1	1	1	1	CGGCGCGTCTCTCAAGCTCGC
229	21	1	1	1	1	1	GGCGCGTCTCTCAAGCTCGCC
230	21	1	1	1	1	1	GCGCGTCTCTCAAGCTCGCCT
231	21	1	1	1	1	1	CGCGTCTCTCAAGCTCGCCTC
232	21	1	1	1	1	1	GCGTCTCTCAAGCTCGCCTCT
233	21	1	1	1	1	1	CGTCTCTCAAGCTCGCCTCTT
234	21	1	1	1	1	1	GTCTCTCAAGCTCGCCTCTTC
235	21	1	1	1	1	1	TCTCTCAAGCTCGCCTCTTCG
236	21	1	1	1	1	1	CTCTCAAGCTCGCCTCTTCGG
237	21	1	1	1	1	1	TCTCAAGCTCGCCTCTTCGGA
238	21	1	1	1	1	1	CTCAAGCTCGCCTCTTCGGAG
239	21	1	1	1	1	1	TCAAGCTCGCCTCTTCGGAGC
240	21	1	1	1	1	1	CAAGCTCGCCTCTTCGGAGCT
241	21	1	1	1	1	1	AAGCTCGCCTCTTCGGAGCTG
242	21	1	1	1	1	1	AGCTCGCCTCTTCGGAGCTGG
243	21	1	1	1	1	1	GCTCGCCTCTTCGGAGCTGGA
244	21	1	1	1	1	1	CTCGCCTCTTCGGAGCTGGAA

FIG. 20 (13)

245	21	1	1	1	1	1	TCGCCTCTTCGGAGCTGGAAC
246	21	1	1	1	1	1	CGCCTCTTCGGAGCTGGAACG
247	21	1	1	1	1	1	GCCTCTTCGGAGCTGGAACGC
248	21	1	1	1	1	1	CCTCTTCGGAGCTGGAACGCC
249	21	1	1	1	1	1	CTCTTCGGAGCTGGAACGCCT
250	21	1	1	1	1	1	TCTTCGGAGCTGGAACGCCTG
251	21	1	1	1	1	1	CTTCGGAGCTGGAACGCCTGA
252	21	1	1	1	1	1	TTCGGAGCTGGAACGCCTGAT
253	21	1	1	1	1	1	TCGGAGCTGGAACGCCTGATT
254	21	1	1	1	1	1	CGGAGCTGGAACGCCTGATTG
255	21	1	1	1	1	1	GGAGCTGGAACGCCTGATTGT
256	21	1	1	1	1	1	GAGCTGGAACGCCTGATTGTC
257	21	1	1	1	1	1	AGCTGGAACGCCTGATTGTCC
258	21	1	1	1	1	1	GCTGGAACGCCTGATTGTCCC
259	21	1	1	1	1	1	CTGGAACGCCTGATTGTCCCC
260	21	1	1	1	1	1	TGGAACGCCTGATTGTCCCCA
261	21	1	1	1	1	1	GGAACGCCTGATTGTCCCCAA
262	21	1	1	1	1	1	GAACGCCTGATTGTCCCCAAC
263	21	1	1	1	1	1	AACGCCTGATTGTCCCCAACA
264	21	1	1	1	1	1	ACGCCTGATTGTCCCCAACAG
265	21	1	1	1	1	1	CGCCTGATTGTCCCCAACAGC

FIG. 20 (14)

266	21	1	1	1	1	1	GCCTGATTGTCCCCAACAGCA
267	21	1	1	1	1	1	CCTGATTGTCCCCAACAGCAA
268	21	1	1	1	1	1	CTGATTGTCCCCAACAGCAAC
269	21	1	1	1	1	1	TGATTGTCCCCAACAGCAACG
270	21	1	1	1	1	1	GATTGTCCCCAACAGCAACGG
271	21	1	1	1	1	1	ATTGTCCCCAACAGCAACGGC
272	21	1	1	1	1	1	TTGTCCCCAACAGCAACGGCG
273	21	1	1	1	1	1	TGTCCCCAACAGCAACGGCGT
274	21	1	1	1	1	1	GTCCCCAACAGCAACGGCGTG
275	21	1	1	1	1	1	TCCCCAACAGCAACGGCGTGA
276	21	1	1	1	1	1	CCCCAACAGCAACGGCGTGAT
277	21	1	1	1	1	1	CCCAACAGCAACGGCGTGATC
278	21	1	1	1	1	1	CCAACAGCAACGGCGTGATCA
279	21	1	1	1	1	1	CAACAGCAACGGCGTGATCAC
280	21	1	1	1	1	1	AACAGCAACGGCGTGATCACG
281	21	1	1	1	1	1	ACAGCAACGGCGTGATCACGA
282	21	1	1	1	1	1	CAGCAACGGCGTGATCACGAC
283	21	1	1	1	1	1	AGCAACGGCGTGATCACGACG
284	21	1	1	1	1	1	GCAACGGCGTGATCACGACGA
285	21	1	1	1	1	1	CAACGGCGTGATCACGACGAC
286	21	1	1	1	1	1	AACGGCGTGATCACGACGACG

FIG. 20 (15)

287	21	1	1	1	1	1	ACGGCGTGATCACGACGACGC
288	21	1	1	1	1	1	CGGCGTGATCACGACGACGCC
289	21	1	1	1	1	1	GGCGTGATCACGACGACGCCT
290	21	1	1	1	1	1	GCGTGATCACGACGACGCCTA
291	21	1	1	1	1	1	CGTGATCACGACGACGCCTAC
292	21	1	1	1	1	1	GTGATCACGACGACGCCTACA
293	21	1	1	1	1	1	TGATCACGACGACGCCTACAC
294	21	1	1	1	1	1	GATCACGACGACGCCTACACC
295	21	1	1	1	1	1	ATCACGACGACGCCTACACCC
296	21	1	1	1	1	1	TCACGACGACGCCTACACCCC
297	21	1	1	1	1	1	CACGACGACGCCTACACCCCC
298	21	1	1	1	1	1	ACGACGACGCCTACACCCCCG
299	21	1	1	1	1	1	CGACGACGCCTACACCCCCGG
300	21	1	1	1	1	1	GACGACGCCTACACCCCCGGG
301	21	1	1	1	1	1	ACGACGCCTACACCCCCGGGA
302	21	1	1	1	1	1	CGACGCCTACACCCCCGGGAC
303	21	1	1	1	1	1	GACGCCTACACCCCCGGGACA
304	21	1	1	1	1	1	ACGCCTACACCCCCGGGACAG
305	21	1	1	1	1	1	CGCCTACACCCCCGGGACAGT
306	21	1	1	1	1	1	GCCTACACCCCCGGGACAGTA
307	21	1	1	1	1	1	CCTACACCCCCGGGACAGTAC
308	21	1	1	1	1	1	CTACACCCCCGGGACAGTACT

FIG. 20 (16)

309	21	1	1	1	1	1	TACACCCCCGGGACAGTACTT
310	21	1	1	1	1	1	ACACCCCCGGGACAGTACTTT
311	21	1	1	1	1	1	CACCCCCGGGACAGTACTTTT
312	21	1	1	1	1	1	ACCCCCGGGACAGTACTTTTA
313	21	1	1	1	1	1	CCCCCGGGACAGTACTTTTAC
314	21	1	1	1	1	1	CCCCGGGACAGTACTTTTACC
315	21	1	1	1	1	1	CCCGGGACAGTACTTTTACCC
316	21	1	1	1	1	1	CCGGGACAGTACTTTTACCCC
317	21	1	1	1	1	1	CGGGACAGTACTTTTACCCCC
318	21	1	1	1	1	1	GGGACAGTACTTTTACCCCCG
319	21	1	1	1	1	1	GGACAGTACTTTTACCCCCGC
320	21	1	1	1	1	1	GACAGTACTTTTACCCCCGCG
321	21	1	1	1	1	1	ACAGTACTTTTACCCCCGCGG
322	21	1	1	1	1	1	CAGTACTTTTACCCCCGCGGG
323	21	1	1	1	1	1	AGTACTTTTACCCCCGCGGGG
324	21	1	1	1	1	1	GTACTTTTACCCCCGCGGGGG
325	21	1	1	1	1	1	TACTTTTACCCCCGCGGGGGT
326	21	1	1	1	1	1	ACTTTTACCCCCGCGGGGGTG
327	21	1	1	1	1	1	CTTTTACCCCCGCGGGGGTGG
328	21	1	1	1	1	1	TTTTACCCCCGCGGGGGTGGC
329	21	1	1	1	1	1	TTTACCCCCGCGGGGGTGGCA

FIG. 20 (17)

330	21	1	1	1	1	1	TTACCCCCGCGGGGGTGGCAG
331	21	1	1	1	1	1	TACCCCCGCGGGGGTGGCAGC
332	21	1	1	1	1	1	ACCCCCGCGGGGGTGGCAGCG
333	21	1	1	1	1	1	CCCCCGCGGGGGTGGCAGCGG
334	21	1	1	1	1	1	CCCCGCGGGGGTGGCAGCGGT
335	21	1	1	1	1	1	CCCGCGGGGGTGGCAGCGGTG
336	21	1	1	1	1	1	CCGCGGGGGTGGCAGCGGTGG
337	21	1	1	1	1	1	CGCGGGGGTGGCAGCGGTGGA
338	21	1	1	1	1	1	GCGGGGGTGGCAGCGGTGGAG
339	21	1	1	1	1	1	CGGGGGTGGCAGCGGTGGAGG
340	21	1	1	1	1	1	GGGGGTGGCAGCGGTGGAGGT
341	21	1	1	1	1	1	GGGGTGGCAGCGGTGGAGGTG
342	21	1	1	1	1	1	GGGTGGCAGCGGTGGAGGTGC
343	21	1	1	1	1	1	GGTGGCAGCGGTGGAGGTGCA
344	21	1	1	1	1	1	GTGGCAGCGGTGGAGGTGCAG
345	21	1	1	1	1	1	TGGCAGCGGTGGAGGTGCAGG
346	21	1	1	1	1	1	GGCAGCGGTGGAGGTGCAGGG
347	21	1	1	1	1	1	GCAGCGGTGGAGGTGCAGGGG
348	21	1	1	1	1	1	CAGCGGTGGAGGTGCAGGGGG
349	21	1	1	1	1	1	AGCGGTGGAGGTGCAGGGGGC
350	21	1	1	1	1	1	GCGGTGGAGGTGCAGGGGGCG

FIG. 20 (18)

351	21	1	1	1	1	1	CGGTGGAGGTGCAGGGGGCGC
352	21	1	1	1	1	1	GGTGGAGGTGCAGGGGGCGCA
353	21	1	1	1	1	1	GTGGAGGTGCAGGGGGCGCAG
354	21	1	1	1	1	1	TGGAGGTGCAGGGGGCGCAGG
355	21	1	1	1	1	1	GGAGGTGCAGGGGGCGCAGGG
356	21	1	1	1	1	1	GAGGTGCAGGGGGCGCAGGGG
357	21	1	1	1	1	1	AGGTGCAGGGGGCGCAGGGGG
358	21	1	1	1	1	1	GGTGCAGGGGGCGCAGGGGGC
359	21	1	1	1	1	1	GTGCAGGGGGCGCAGGGGGCG
360	21	1	1	1	1	1	TGCAGGGGGCGCAGGGGGCGG
361	21	1	1	1	1	1	GCAGGGGGCGCAGGGGGCGGC
362	21	1	1	1	1	1	CAGGGGGCGCAGGGGGCGGCG
363	21	1	1	1	1	1	AGGGGGCGCAGGGGGCGGCGT
364	21	1	1	1	1	1	GGGGGCGCAGGGGGCGGCGTC
365	21	1	1	1	1	1	GGGGCGCAGGGGGCGGCGTCA
366	21	1	1	1	1	1	GGGCGCAGGGGGCGGCGTCAC
367	21	1	1	1	1	1	GGCGCAGGGGGCGGCGTCACC
368	21	1	1	1	1	1	GCGCAGGGGGCGGCGTCACCG
369	21	1	1	1	1	1	CGCAGGGGGCGGCGTCACCGA
370	21	1	2	2	2	2	GCAGGGGGCGGCGTCACCGAG
371	21	2	2	2	2	2	CAGGGGGCGGCGTCACCGAGG
372	21	2	2	2	2	2	AGGGGGCGGCGTCACCGAGGA

FIG. 20 (19)

373	21	2	2	2	2	2	GGGGGCGGCGTCACCGAGGAG
374	21	2	2	2	2	2	GGGGCGGCGTCACCGAGGAGC
375	21	2	2	2	2	2	GGGCGGCGTCACCGAGGAGCA
376	21	2	2	2	2	2	GGCGGCGTCACCGAGGAGCAG
377	21	2	2	2	2	2	GCGGCGTCACCGAGGAGCAGG
378	21	2	2	2	2	2	CGGCGTCACCGAGGAGCAGGA
379	21	2	2	2	2	2	GGCGTCACCGAGGAGCAGGAG
380	21	2	2	2	2	2	GCGTCACCGAGGAGCAGGAGG
381	21	2	2	2	2	2	CGTCACCGAGGAGCAGGAGGG
382	21	2	2	2	2	2	GTCACCGAGGAGCAGGAGGGC
383	21	2	2	2	2	2	TCACCGAGGAGCAGGAGGGCT
384	21	2	2	2	2	2	CACCGAGGAGCAGGAGGGCTT
385	21	1	3	3	3	3	ACCGAGGAGCAGGAGGGCTTC
386	21	1	3	3	3	3	CCGAGGAGCAGGAGGGCTTCG
387	21	1	3	3	3	3	CGAGGAGCAGGAGGGCTTCGC
388	21	1	2	2	2	2	GAGGAGCAGGAGGGCTTCGCC
389	21	1	2	2	2	2	AGGAGCAGGAGGGCTTCGCCG
390	21	1	2	2	2	2	GGAGCAGGAGGGCTTCGCCGA
391	21	1	2	2	2	2	GAGCAGGAGGGCTTCGCCGAC
392	21	1	2	2	2	2	AGCAGGAGGGCTTCGCCGACG
393	21	1	2	2	2	2	GCAGGAGGGCTTCGCCGACGG

FIG. 20 (20)

394	21	1	2	2	2	2	CAGGAGGGCTTCGCCGACGGC
395	21	1	2	2	2	2	AGGAGGGCTTCGCCGACGGCT
396	21	1	2	2	2	2	GGAGGGCTTCGCCGACGGCTT
397	21	1	1	1	1	1	GAGGGCTTCGCCGACGGCTTT
398	21	1	1	1	1	1	AGGGCTTCGCCGACGGCTTTG
399	21	1	1	1	1	1	GGGCTTCGCCGACGGCTTTGT
400	21	1	1	1	1	1	GGCTTCGCCGACGGCTTTGTC
401	21	1	1	1	1	1	GCTTCGCCGACGGCTTTGTCA
402	21	1	1	1	1	1	CTTCGCCGACGGCTTTGTCAA
403	21	1	1	1	1	1	TTCGCCGACGGCTTTGTCAAA
404	21	1	1	1	1	1	TCGCCGACGGCTTTGTCAAAG
405	21	1	1	1	1	1	CGCCGACGGCTTTGTCAAAGC
406	21	1	1	1	1	1	GCCGACGGCTTTGTCAAAGCC
407	21	1	1	1	1	1	CCGACGGCTTTGTCAAAGCCC
408	21	1	1	1	1	1	CGACGGCTTTGTCAAAGCCCT
409	21	1	2	2	2	2	GACGGCTTTGTCAAAGCCCTG
410	21	1	2	2	2	2	ACGGCTTTGTCAAAGCCCTGG
411	21	1	2	2	2	2	CGGCTTTGTCAAAGCCCTGGA
412	21	1	2	2	2	2	GGCTTTGTCAAAGCCCTGGAC
413	21	1	2	2	2	2	GCTTTGTCAAAGCCCTGGACG
414	21	1	2	2	2	2	CTTTGTCAAAGCCCTGGACGA

FIG. 20 (21)

415	21	1	2	2	2	2	TTTGTCAAAGCCCTGGACGAT
416	21	1	2	2	2	2	TTGTCAAAGCCCTGGACGATC
417	21	1	2	2	2	2	TGTCAAAGCCCTGGACGATCT
418	21	1	2	2	2	2	GTCAAAGCCCTGGACGATCTG
419	21	1	2	2	2	2	TCAAAGCCCTGGACGATCTGC
420	21	1	2	2	2	2	CAAAGCCCTGGACGATCTGCA
421	21	1	2	2	2	2	AAAGCCCTGGACGATCTGCAC
422	21	1	2	2	2	2	AAGCCCTGGACGATCTGCACA
423	21	1	2	2	2	2	AGCCCTGGACGATCTGCACAA
424	21	1	2	2	2	2	GCCCTGGACGATCTGCACAAG
425	21	1	2	2	2	2	CCCTGGACGATCTGCACAAGA
426	21	1	2	2	2	2	CCTGGACGATCTGCACAAGAT
427	21	1	2	2	2	2	CTGGACGATCTGCACAAGATG
428	21	1	2	2	2	2	TGGACGATCTGCACAAGATGA
429	21	1	2	2	2	2	GGACGATCTGCACAAGATGAA
430	21	1	2	2	2	2	GACGATCTGCACAAGATGAAC
431	21	1	2	2	2	2	ACGATCTGCACAAGATGAACC
432	21	1	2	2	2	2	CGATCTGCACAAGATGAACCA
433	21	1	2	2	2	2	GATCTGCACAAGATGAACCAC
434	21	1	2	2	2	2	ATCTGCACAAGATGAACCACG
435	21	1	2	2	2	2	TCTGCACAAGATGAACCACGT
436	21	2	2	2	2	2	CTGCACAAGATGAACCACGTG

FIG. 20 (22)

437	21	2	2	2	2	2	TGCACAAGATGAACCACGTGA
438	21	2	2	2	2	2	GCACAAGATGAACCACGTGAC
439	21	1	2	2	2	2	CACAAGATGAACCACGTGACA
440	21	1	2	2	2	2	ACAAGATGAACCACGTGACAC
441	21	1	2	2	2	2	CAAGATGAACCACGTGACACC
442	21	1	2	2	2	2	AAGATGAACCACGTGACACCC
443	21	1	2	2	2	2	AGATGAACCACGTGACACCCC
444	21	1	2	2	2	2	GATGAACCACGTGACACCCCC
445	21	1	2	2	2	2	ATGAACCACGTGACACCCCCC
446	21	1	2	2	2	2	TGAACCACGTGACACCCCCCA
447	21	1	2	2	2	2	GAACCACGTGACACCCCCCAA
448	21	1	2	2	2	2	AACCACGTGACACCCCCCAAC
449	21	1	2	2	2	2	ACCACGTGACACCCCCCAACG
450	21	1	2	2	2	2	CCACGTGACACCCCCCAACGT
451	21	1	2	2	2	2	CACGTGACACCCCCCAACGTG
452	21	1	2	2	2	2	ACGTGACACCCCCCAACGTGT
453	21	1	2	2	2	2	CGTGACACCCCCCAACGTGTC
454	21	1	2	2	2	2	GTGACACCCCCCAACGTGTCC
455	21	1	2	2	2	2	TGACACCCCCCAACGTGTCCC
456	21	1	2	2	2	2	GACACCCCCCAACGTGTCCCT
457	21	1	2	2	2	2	ACACCCCCCAACGTGTCCCTG

FIG. 20 (23)

458	21	1	2	2	2	2	CACCCCCCAACGTGTCCCTGG
459	21	1	2	2	2	2	ACCCCCCAACGTGTCCCTGGG
460	21	2	2	2	2	2	CCCCCCAACGTGTCCCTGGGC
461	21	2	2	2	2	2	CCCCCAACGTGTCCCTGGGCG
462	21	2	2	2	2	2	CCCCAACGTGTCCCTGGGCGC
463	21	1	2	2	2	2	CCCAACGTGTCCCTGGGCGCT
464	21	1	2	2	2	2	CCAACGTGTCCCTGGGCGCTA
465	21	1	1	1	1	1	CAACGTGTCCCTGGGCGCTAC
466	21	1	1	1	1	1	AACGTGTCCCTGGGCGCTACC
467	21	1	1	1	1	1	ACGTGTCCCTGGGCGCTACCG
468	21	1	1	1	1	1	CGTGTCCCTGGGCGCTACCGG
469	21	1	1	1	1	1	GTGTCCCTGGGCGCTACCGGG
470	21	1	1	1	1	1	TGTCCCTGGGCGCTACCGGGG
471	21	1	1	1	1	1	GTCCCTGGGCGCTACCGGGGG
472	21	1	1	1	1	1	TCCCTGGGCGCTACCGGGGGG
473	21	1	1	1	1	1	CCCTGGGCGCTACCGGGGGGC
474	21	1	1	1	1	1	CCTGGGCGCTACCGGGGGGCC
475	21	1	1	1	1	1	CTGGGCGCTACCGGGGGGCCC
476	21	1	1	1	1	1	TGGGCGCTACCGGGGGGCCCC
477	21	1	1	1	1	1	GGGCGCTACCGGGGGGCCCCC
478	21	1	1	1	1	1	GGCGCTACCGGGGGGCCCCCG

FIG. 20 (24)

479	21	1	1	1	1	1	GCGCTACCGGGGGGCCCCCGG
480	21	1	1	1	1	1	CGCTACCGGGGGGCCCCCGGC
481	21	1	1	1	1	1	GCTACCGGGGGGCCCCCGGCT
482	21	1	1	1	1	1	CTACCGGGGGGCCCCCGGCTG
483	21	1	1	1	1	1	TACCGGGGGGCCCCCGGCTGG
484	21	1	1	1	1	1	ACCGGGGGGCCCCCGGCTGGG
485	21	1	1	1	1	1	CCGGGGGGCCCCCGGCTGGGC
486	21	1	1	1	1	1	CGGGGGGCCCCCGGCTGGGCC
487	21	1	1	1	1	1	GGGGGGCCCCCGGCTGGGCCC
488	21	1	1	1	1	1	GGGGGCCCCCGGCTGGGCCCG
489	21	1	1	1	1	1	GGGGCCCCCGGCTGGGCCCGG
490	21	1	1	1	1	1	GGGCCCCCGGCTGGGCCCGGG
491	21	1	1	1	1	1	GGCCCCCGGCTGGGCCCGGGG
492	21	1	1	1	1	1	GCCCCCGGCTGGGCCCGGGGG
493	21	1	1	1	1	1	CCCCCGGCTGGGCCCGGGGGC
494	21	1	1	1	1	1	CCCCGGCTGGGCCCGGGGGCG
495	21	1	1	1	1	1	CCCGGCTGGGCCCGGGGGCGT
496	21	1	1	1	1	1	CCGGCTGGGCCCGGGGGCGTC
497	21	1	1	1	1	1	CGGCTGGGCCCGGGGGCGTCT
498	21	1	1	1	1	1	GGCTGGGCCCGGGGGCGTCTA
499	21	1	1	1	1	1	GCTGGGCCCGGGGGCGTCTAC
500	21	1	1	1	1	1	CTGGGCCCGGGGGCGTCTACG

FIG. 20 (25)

501	21	1	1	1	1	1	TGGGCCCGGGGGCGTCTACGC
502	21	1	1	1	1	1	GGGCCCGGGGGCGTCTACGCC
503	21	1	1	1	1	1	GGCCCGGGGGCGTCTACGCCG
504	21	1	1	1	1	1	GCCCGGGGGCGTCTACGCCGG
505	21	1	1	1	1	1	CCCGGGGGCGTCTACGCCGGC
506	21	1	1	1	1	1	CCGGGGGCGTCTACGCCGGCC
507	21	1	1	1	1	1	CGGGGGCGTCTACGCCGGCCC
508	21	1	1	1	1	1	GGGGGCGTCTACGCCGGCCCG
509	21	1	1	1	1	1	GGGGCGTCTACGCCGGCCCGG
510	21	1	1	1	1	1	GGGCGTCTACGCCGGCCCGGA
511	21	1	1	1	1	1	GGCGTCTACGCCGGCCCGGAG
512	21	1	1	1	1	1	GCGTCTACGCCGGCCCGGAGC
513	21	1	1	1	1	1	CGTCTACGCCGGCCCGGAGCC
514	21	1	1	1	1	1	GTCTACGCCGGCCCGGAGCCA
515	21	1	1	1	1	1	TCTACGCCGGCCCGGAGCCAC
516	21	1	1	1	1	1	CTACGCCGGCCCGGAGCCACC
517	21	1	1	1	1	1	TACGCCGGCCCGGAGCCACCT
518	21	1	1	1	1	1	ACGCCGGCCCGGAGCCACCTC
519	21	1	1	1	1	1	CGCCGGCCCGGAGCCACCTCC
520	21	1	1	1	1	1	GCCGGCCCGGAGCCACCTCCC
521	21	1	1	1	1	1	CCGGCCCGGAGCCACCTCCCG

FIG. 20 (26)

522	21	1	1	1	1	1	CGGCCCGGAGCCACCTCCCGT
523	21	1	1	1	1	1	GGCCCGGAGCCACCTCCCGTT
524	21	1	1	1	1	1	GCCCGGAGCCACCTCCCGTTT
525	21	1	1	1	1	1	CCCGGAGCCACCTCCCGTTTA
526	21	1	1	1	1	1	CCGGAGCCACCTCCCGTTTAC
527	21	1	1	1	1	1	CGGAGCCACCTCCCGTTTACA
528	21	1	1	1	1	1	GGAGCCACCTCCCGTTTACAC
529	21	1	1	1	1	1	GAGCCACCTCCCGTTTACACC
530	21	1	1	1	1	1	AGCCACCTCCCGTTTACACCA
531	21	1	1	1	1	1	GCCACCTCCCGTTTACACCAA
532	21	1	1	1	1	1	CCACCTCCCGTTTACACCAAC
533	21	1	1	1	1	1	CACCTCCCGTTTACACCAACC
534	21	1	1	1	1	1	ACCTCCCGTTTACACCAACCT
535	21	1	2	2	2	2	CCTCCCGTTTACACCAACCTC
536	21	1	2	2	2	2	CTCCCGTTTACACCAACCTCA
537	21	1	2	2	2	2	TCCCGTTTACACCAACCTCAG
538	21	1	2	2	2	2	CCCGTTTACACCAACCTCAGC
539	21	1	2	2	2	2	CCGTTTACACCAACCTCAGCA
540	21	1	2	2	2	2	CGTTTACACCAACCTCAGCAG
541	21	1	1	1	1	1	GTTTACACCAACCTCAGCAGC
542	21	1	1	1	1	1	TTTACACCAACCTCAGCAGCT

FIG. 20 (27)

543	21	1	1	1	1	1	TTACACCAACCTCAGCAGCTA
544	21	1	2	2	2	2	TACACCAACCTCAGCAGCTAC
545	21	1	2	2	2	2	ACACCAACCTCAGCAGCTACT
546	21	1	2	2	2	2	CACCAACCTCAGCAGCTACTC
547	21	1	1	1	1	1	ACCAACCTCAGCAGCTACTCC
548	21	1	1	1	1	1	CCAACCTCAGCAGCTACTCCC
549	21	1	1	1	1	1	CAACCTCAGCAGCTACTCCCC
550	21	1	1	1	1	1	AACCTCAGCAGCTACTCCCCA
551	21	1	1	1	1	1	ACCTCAGCAGCTACTCCCCAG
552	21	1	1	1	1	1	CCTCAGCAGCTACTCCCCAGC
553	21	1	1	1	1	1	CTCAGCAGCTACTCCCCAGCC
554	21	1	1	1	1	1	TCAGCAGCTACTCCCCAGCCT
555	21	1	1	1	1	1	CAGCAGCTACTCCCCAGCCTC
556	21	1	1	1	1	1	AGCAGCTACTCCCCAGCCTCT
557	21	1	1	1	1	1	GCAGCTACTCCCCAGCCTCTG
558	21	1	1	1	1	1	CAGCTACTCCCCAGCCTCTGC
559	21	1	1	1	1	1	AGCTACTCCCCAGCCTCTGCG
560	21	1	1	1	1	1	GCTACTCCCCAGCCTCTGCGT
561	21	1	1	1	1	1	CTACTCCCCAGCCTCTGCGTC
562	21	1	1	1	1	1	TACTCCCCAGCCTCTGCGTCC
563	21	1	1	1	1	1	ACTCCCCAGCCTCTGCGTCCT
564	21	1	1	1	1	1	CTCCCCAGCCTCTGCGTCCTC

FIG. 20 (28)

565	21	1	1	1	1	1	TCCCCAGCCTCTGCGTCCTCG
566	21	1	1	1	1	1	CCCCAGCCTCTGCGTCCTCGG
567	21	1	1	1	1	1	CCCAGCCTCTGCGTCCTCGGG
568	21	1	1	1	1	1	CCAGCCTCTGCGTCCTCGGGA
569	21	1	1	1	1	1	CAGCCTCTGCGTCCTCGGGAG
570	21	1	1	1	1	1	AGCCTCTGCGTCCTCGGGAGG
571	21	1	1	1	1	1	GCCTCTGCGTCCTCGGGAGGC
572	21	1	1	1	1	1	CCTCTGCGTCCTCGGGAGGCG
573	21	1	1	1	1	1	CTCTGCGTCCTCGGGAGGCGC
574	21	1	1	1	1	1	TCTGCGTCCTCGGGAGGCGCC
575	21	1	1	1	1	1	CTGCGTCCTCGGGAGGCGCCG
576	21	1	1	1	1	1	TGCGTCCTCGGGAGGCGCCGG
577	21	1	1	1	1	1	GCGTCCTCGGGAGGCGCCGGG
578	21	1	1	1	1	1	CGTCCTCGGGAGGCGCCGGGG
579	21	1	1	1	1	1	GTCCTCGGGAGGCGCCGGGGC
580	21	1	1	1	1	1	TCCTCGGGAGGCGCCGGGGCT
581	21	1	1	1	1	1	CCTCGGGAGGCGCCGGGGCTG
582	21	1	1	1	1	1	CTCGGGAGGCGCCGGGGCTGC
583	21	1	1	1	1	1	TCGGGAGGCGCCGGGGCTGCC
584	21	1	1	1	1	1	CGGGAGGCGCCGGGGCTGCCG
585	21	1	1	1	1	1	GGGAGGCGCCGGGGCTGCCGT

FIG. 20 (29)

586	21	1	1	1	1	1	GGAGGCGCCGGGGCTGCCGTC
587	21	1	1	1	1	1	GAGGCGCCGGGGCTGCCGTCG
588	21	1	1	1	1	1	AGGCGCCGGGGCTGCCGTCGG
589	21	1	1	1	1	1	GGCGCCGGGGCTGCCGTCGGG
590	21	1	1	1	1	1	GCGCCGGGGCTGCCGTCGGGA
591	21	1	1	1	1	1	CGCCGGGGCTGCCGTCGGGAC
592	21	1	1	1	1	1	GCCGGGGCTGCCGTCGGGACC
593	21	1	1	1	1	1	CCGGGGCTGCCGTCGGGACCG
594	21	1	1	1	1	1	CGGGGCTGCCGTCGGGACCGG
595	21	1	1	1	1	1	GGGGCTGCCGTCGGGACCGGG
596	21	1	1	1	1	1	GGGCTGCCGTCGGGACCGGGA
597	21	1	1	1	1	1	GGCTGCCGTCGGGACCGGGAG
598	21	1	1	1	1	1	GCTGCCGTCGGGACCGGGAGC
599	21	1	1	1	1	1	CTGCCGTCGGGACCGGGAGCT
600	21	1	1	1	1	1	TGCCGTCGGGACCGGGAGCTC
601	21	1	1	1	1	1	GCCGTCGGGACCGGGAGCTCG
602	21	1	1	1	1	1	CCGTCGGGACCGGGAGCTCGT
603	21	1	1	1	1	1	CGTCGGGACCGGGAGCTCGTA
604	21	1	1	1	1	1	GTCGGGACCGGGAGCTCGTAC
605	21	1	1	1	1	1	TCGGGACCGGGAGCTCGTACC
606	21	1	1	1	1	1	CGGGACCGGGAGCTCGTACCC

FIG. 20 (30)

607	21	1	1	1	1	1	GGGACCGGGAGCTCGTACCCG
608	21	1	1	1	1	1	GGACCGGGAGCTCGTACCCGA
609	21	1	1	1	1	1	GACCGGGAGCTCGTACCCGAC
610	21	1	1	1	1	1	ACCGGGAGCTCGTACCCGACG
611	21	1	1	1	1	1	CCGGGAGCTCGTACCCGACGA
612	21	1	1	1	1	1	CGGGAGCTCGTACCCGACGAC
613	21	1	1	1	1	1	GGGAGCTCGTACCCGACGACC
614	21	1	1	1	1	1	GGAGCTCGTACCCGACGACCA
615	21	1	1	1	1	1	GAGCTCGTACCCGACGACCAC
616	21	1	1	1	1	1	AGCTCGTACCCGACGACCACC
617	21	1	1	1	1	1	GCTCGTACCCGACGACCACCA
618	21	1	1	1	1	1	CTCGTACCCGACGACCACCAT
619	21	1	1	1	1	1	TCGTACCCGACGACCACCATC
620	21	1	1	1	1	1	CGTACCCGACGACCACCATCA
621	21	1	1	1	1	1	GTACCCGACGACCACCATCAG
622	21	1	2	2	2	2	TACCCGACGACCACCATCAGC
623	21	1	2	2	2	2	ACCCGACGACCACCATCAGCT
624	21	1	2	2	2	2	CCCGACGACCACCATCAGCTA
625	21	1	2	2	2	2	CCGACGACCACCATCAGCTAC
626	21	1	2	2	2	2	CGACGACCACCATCAGCTACC
627	21	1	2	2	2	2	GACGACCACCATCAGCTACCT
628	21	1	2	2	2	2	ACGACCACCATCAGCTACCTC

FIG. 20 (31)

629	21	1	2	2	2	2	CGACCACCATCAGCTACCTCC
630	21	1	2	2	2	2	GACCACCATCAGCTACCTCCC
631	21	1	2	2	2	2	ACCACCATCAGCTACCTCCCA
632	21	2	2	2	2	2	CCACCATCAGCTACCTCCCAC
633	21	2	2	2	2	2	CACCATCAGCTACCTCCCACA
634	21	1	2	2	2	2	ACCATCAGCTACCTCCCACAC
635	21	1	2	2	2	2	CCATCAGCTACCTCCCACACG
636	21	1	2	2	2	2	CATCAGCTACCTCCCACACGC
637	21	1	1	1	1	1	ATCAGCTACCTCCCACACGCG
638	21	1	1	1	1	1	TCAGCTACCTCCCACACGCGC
639	21	1	1	1	1	1	CAGCTACCTCCCACACGCGCC
640	21	1	1	1	1	1	AGCTACCTCCCACACGCGCCG
641	21	1	1	1	1	1	GCTACCTCCCACACGCGCCGC
642	21	1	1	1	1	1	CTACCTCCCACACGCGCCGCC
643	21	1	1	1	1	1	TACCTCCCACACGCGCCGCCC
644	21	1	1	1	1	1	ACCTCCCACACGCGCCGCCCT
645	21	1	1	1	1	1	CCTCCCACACGCGCCGCCCTT
646	21	1	1	1	1	1	CTCCCACACGCGCCGCCCTTC
647	21	1	1	1	1	1	TCCCACACGCGCCGCCCTTCG
648	21	1	1	1	1	1	CCCACACGCGCCGCCCTTCGC
649	21	1	1	1	1	1	CCACACGCGCCGCCCTTCGCC

FIG. 20 (32)

650	21	1	1	1	1	1	CACACGCGCCGCCCTTCGCCG
651	21	1	1	1	1	1	ACACGCGCCGCCCTTCGCCGG
652	21	1	1	1	1	1	CACGCGCCGCCCTTCGCCGGT
653	21	1	1	1	1	1	ACGCGCCGCCCTTCGCCGGTG
654	21	1	1	1	1	1	CGCGCCGCCCTTCGCCGGTGG
655	21	1	1	1	1	1	GCGCCGCCCTTCGCCGGTGGC
656	21	1	1	1	1	1	CGCCGCCCTTCGCCGGTGGCC
657	21	1	1	1	1	1	GCCGCCCTTCGCCGGTGGCCA
658	21	1	1	1	1	1	CCGCCCTTCGCCGGTGGCCAC
659	21	1	1	1	1	1	CGCCCTTCGCCGGTGGCCACC
660	21	1	1	1	1	1	GCCCTTCGCCGGTGGCCACCC
661	21	1	1	1	1	1	CCCTTCGCCGGTGGCCACCCG
662	21	1	1	1	1	1	CCTTCGCCGGTGGCCACCCGG
663	21	1	1	1	1	1	CTTCGCCGGTGGCCACCCGGC
664	21	1	1	1	1	1	TTCGCCGGTGGCCACCCGGCG
665	21	1	1	1	1	1	TCGCCGGTGGCCACCCGGCGC
666	21	1	1	1	1	1	CGCCGGTGGCCACCCGGCGCA
667	21	1	1	1	1	1	GCCGGTGGCCACCCGGCGCAG
668	21	1	1	1	1	1	CCGGTGGCCACCCGGCGCAGC
669	21	1	1	1	1	1	CGGTGGCCACCCGGCGCAGCT
670	21	1	1	1	1	1	GGTGGCCACCCGGCGCAGCTG

FIG. 20 (33)

671	21	1	1	1	1	1	GTGGCCACCCGGCGCAGCTGG
672	21	1	1	1	1	1	TGGCCACCCGGCGCAGCTGGG
673	21	1	1	1	1	1	GGCCACCCGGCGCAGCTGGGC
674	21	1	1	1	1	1	GCCACCCGGCGCAGCTGGGCT
675	21	1	1	1	1	1	CCACCCGGCGCAGCTGGGCTT
676	21	1	1	1	1	1	CACCCGGCGCAGCTGGGCTTG
677	21	1	1	1	1	1	ACCCGGCGCAGCTGGGCTTGG
678	21	1	1	1	1	1	CCCGGCGCAGCTGGGCTTGGG
679	21	1	1	1	1	1	CCGGCGCAGCTGGGCTTGGGC
680	21	1	1	1	1	1	CGGCGCAGCTGGGCTTGGGCC
681	21	1	1	1	1	1	GGCGCAGCTGGGCTTGGGCCG
682	21	1	1	1	1	1	GCGCAGCTGGGCTTGGGCCGC
683	21	1	1	1	1	1	CGCAGCTGGGCTTGGGCCGCG
684	21	1	1	1	1	1	GCAGCTGGGCTTGGGCCGCGG
685	21	1	1	1	1	1	CAGCTGGGCTTGGGCCGCGGC
686	21	1	1	1	1	1	AGCTGGGCTTGGGCCGCGGCG
687	21	1	1	1	1	1	GCTGGGCTTGGGCCGCGGCGC
688	21	1	1	1	1	1	CTGGGCTTGGGCCGCGGCGCC
689	21	1	1	1	1	1	TGGGCTTGGGCCGCGGCGCCT
690	21	1	1	1	1	1	GGGCTTGGGCCGCGGCGCCTC
691	21	1	1	1	1	1	GGCTTGGGCCGCGGCGCCTCC
692	21	1	1	1	1	1	GCTTGGGCCGCGGCGCCTCCA

FIG. 20 (34)

693	21	1	1	1	1	1	CTTGGGCCGCGGCGCCTCCAC
694	21	1	1	1	1	1	TTGGGCCGCGGCGCCTCCACC
695	21	1	1	1	1	1	TGGGCCGCGGCGCCTCCACCT
696	21	1	1	1	1	1	GGGCCGCGGCGCCTCCACCTT
697	21	1	1	1	1	1	GGCCGCGGCGCCTCCACCTTC
698	21	1	1	1	1	1	GCCGCGGCGCCTCCACCTTCA
699	21	1	1	1	1	1	CCGCGGCGCCTCCACCTTCAA
700	21	1	1	1	1	1	CGCGGCGCCTCCACCTTCAAG
701	21	1	1	1	1	1	GCGGCGCCTCCACCTTCAAGG
702	21	1	1	1	1	1	CGGCGCCTCCACCTTCAAGGA
703	21	1	1	1	1	1	GGCGCCTCCACCTTCAAGGAG
704	21	1	1	1	1	1	GCGCCTCCACCTTCAAGGAGG
705	21	1	1	1	1	1	CGCCTCCACCTTCAAGGAGGA
706	21	1	1	1	1	1	GCCTCCACCTTCAAGGAGGAA
707	21	1	1	1	1	1	CCTCCACCTTCAAGGAGGAAC
708	21	1	1	1	1	1	CTCCACCTTCAAGGAGGAACC
709	21	1	1	1	1	1	TCCACCTTCAAGGAGGAACCG
710	21	1	1	1	1	1	CCACCTTCAAGGAGGAACCGC
711	21	1	1	1	1	1	CACCTTCAAGGAGGAACCGCA
712	21	1	1	1	1	1	ACCTTCAAGGAGGAACCGCAG
713	21	1	1	1	1	1	CCTTCAAGGAGGAACCGCAGA

FIG. 20 (35)

714	21	1	1	1	1	1	CTTCAAGGAGGAACCGCAGAC
715	21	1	1	1	1	1	TTCAAGGAGGAACCGCAGACC
716	21	1	1	1	1	1	TCAAGGAGGAACCGCAGACCG
717	21	1	1	1	1	1	CAAGGAGGAACCGCAGACCGT
718	21	1	1	1	1	1	AAGGAGGAACCGCAGACCGTG
719	21	1	1	1	1	1	AGGAGGAACCGCAGACCGTGC
720	21	1	1	1	1	1	GGAGGAACCGCAGACCGTGCC
721	21	1	2	2	2	2	GAGGAACCGCAGACCGTGCCG
722	21	1	2	2	2	2	AGGAACCGCAGACCGTGCCGG
723	21	1	2	2	2	2	GGAACCGCAGACCGTGCCGGA
724	21	1	3	3	3	3	GAACCGCAGACCGTGCCGGAG
725	21	1	2	2	2	2	AACCGCAGACCGTGCCGGAGG
726	21	1	2	2	2	2	ACCGCAGACCGTGCCGGAGGC
727	21	1	1	1	1	1	CCGCAGACCGTGCCGGAGGCG
728	21	1	1	1	1	1	CGCAGACCGTGCCGGAGGCGC
729	21	1	1	1	1	1	GCAGACCGTGCCGGAGGCGCG
730	21	1	1	1	1	1	CAGACCGTGCCGGAGGCGCGC
731	21	1	1	1	1	1	AGACCGTGCCGGAGGCGCGCA
732	21	1	1	1	1	1	GACCGTGCCGGAGGCGCGCAG
733	21	1	1	1	1	1	ACCGTGCCGGAGGCGCGCAGC
734	21	1	1	1	1	1	CCGTGCCGGAGGCGCGCAGCC

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FIG. 20 (36)

735	21	1	1	1	1	1	CGTGCCGGAGGCGCGCAGCCG
736	21	1	1	1	1	1	GTGCCGGAGGCGCGCAGCCGG
737	21	1	1	1	1	1	TGCCGGAGGCGCGCAGCCGGG
738	21	1	1	1	1	1	GCCGGAGGCGCGCAGCCGGGA
739	21	1	1	1	1	1	CCGGAGGCGCGCAGCCGGGAC
740	21	1	1	1	1	1	CGGAGGCGCGCAGCCGGGACG
741	21	1	1	1	1	1	GGAGGCGCGCAGCCGGGACGC
742	21	1	1	1	1	1	GAGGCGCGCAGCCGGGACGCC
743	21	1	1	1	1	1	AGGCGCGCAGCCGGGACGCCA
744	21	1	1	1	1	1	GGCGCGCAGCCGGGACGCCAC
745	21	1	1	1	1	1	GCGCGCAGCCGGGACGCCACG
746	21	1	1	1	1	1	CGCGCAGCCGGGACGCCACGC
747	21	1	1	1	1	1	GCGCAGCCGGGACGCCACGCC
748	21	1	2	2	2	2	CGCAGCCGGGACGCCACGCCG
749	21	1	2	2	2	2	GCAGCCGGGACGCCACGCCGC
750	21	1	2	2	2	2	CAGCCGGGACGCCACGCCGCC
751	21	1	1	1	1	1	AGCCGGGACGCCACGCCGCCG
752	21	1	1	1	1	1	GCCGGGACGCCACGCCGCCGG
753	21	1	1	1	1	1	CCGGGACGCCACGCCGCCGGT
754	21	1	1	1	1	1	CGGGACGCCACGCCGCCGGTG
755	21	1	1	1	1	1	GGGACGCCACGCCGCCGGTGT
756	21	1	1	1	1	1	GGACGCCACGCCGCCGGTGTC

FIG. 20 (37)

757	21	1	2	2	2	2	GACGCCACGCCGCCGGTGTCC
758	21	1	2	2	2	2	ACGCCACGCCGCCGGTGTCCC
759	21	1	2	2	2	2	CGCCACGCCGCCGGTGTCCCC
760	21	1	2	2	2	2	GCCACGCCGCCGGTGTCCCCC
761	21	1	2	2	2	2	CCACGCCGCCGGTGTCCCCCA
762	21	1	2	2	2	2	CACGCCGCCGGTGTCCCCCAT
763	21	1	2	2	2	2	ACGCCGCCGGTGTCCCCCATC
764	21	1	2	2	2	2	CGCCGCCGGTGTCCCCCATCA
765	21	1	2	2	2	2	GCCGCCGGTGTCCCCCATCAA
766	21	1	2	2	2	2	CCGCCGGTGTCCCCCATCAAC
767	21	1	2	2	2	2	CGCCGGTGTCCCCCATCAACA
768	21	1	2	2	2	2	GCCGGTGTCCCCCATCAACAT
769	21	1	2	2	2	2	CCGGTGTCCCCCATCAACATG
770	21	1	2	2	2	2	CGGTGTCCCCCATCAACATGG
771	21	1	2	2	2	2	GGTGTCCCCCATCAACATGGA
772	21	2	2	2	2	2	GTGTCCCCCATCAACATGGAA
773	21	2	2	2	2	2	TGTCCCCCATCAACATGGAAG
774	21	2	2	2	2	2	GTCCCCCATCAACATGGAAGA
775	21	2	2	2	2	2	TCCCCCATCAACATGGAAGAC
776	21	2	2	2	2	2	CCCCCATCAACATGGAAGACC
777	21	2	2	2	2	2	CCCCATCAACATGGAAGACCA

FIG. 20 (38)

778	21	1	2	2	2	2	CCCATCAACATGGAAGACCAA
779	21	1	2	2	2	2	CCATCAACATGGAAGACCAAG
780	21	1	2	2	2	2	CATCAACATGGAAGACCAAGA
781	21	1	2	2	2	2	ATCAACATGGAAGACCAAGAG
782	21	1	2	2	2	2	TCAACATGGAAGACCAAGAGC
783	21	1	2	2	2	2	CAACATGGAAGACCAAGAGCG
784	21	1	2	2	2	2	AACATGGAAGACCAAGAGCGC
785	21	1	2	2	2	2	ACATGGAAGACCAAGAGCGCA
786	21	1	2	2	2	2	CATGGAAGACCAAGAGCGCAT
787	21	1	2	2	2	2	ATGGAAGACCAAGAGCGCATC
788	21	1	2	2	2	2	TGGAAGACCAAGAGCGCATCA
789	21	1	2	2	2	2	GGAAGACCAAGAGCGCATCAA
790	21	1	2	2	2	2	GAAGACCAAGAGCGCATCAAA
791	21	1	2	2	2	2	AAGACCAAGAGCGCATCAAAG
792	21	1	2	2	2	2	AGACCAAGAGCGCATCAAAGT
793	21	1	2	2	2	2	GACCAAGAGCGCATCAAAGTG
794	21	1	2	2	2	2	ACCAAGAGCGCATCAAAGTGG
795	21	1	2	2	2	2	CCAAGAGCGCATCAAAGTGGA
796	21	1	2	2	2	2	CAAGAGCGCATCAAAGTGGAG
797	21	1	2	2	2	2	AAGAGCGCATCAAAGTGGAGC
798	21	1	2	2	2	2	AGAGCGCATCAAAGTGGAGCG

FIG. 20 (39)

799	21	1	2	2	2	2	GAGCGCATCAAAGTGGAGCGC
800	21	1	2	2	2	2	AGCGCATCAAAGTGGAGCGCA
801	21	1	2	2	2	2	GCGCATCAAAGTGGAGCGCAA
802	21	1	2	2	2	2	CGCATCAAAGTGGAGCGCAAG
803	21	1	2	2	2	2	GCATCAAAGTGGAGCGCAAGC
804	21	1	2	2	2	2	CATCAAAGTGGAGCGCAAGCG
805	21	1	2	2	2	2	ATCAAAGTGGAGCGCAAGCGG
806	21	1	2	2	2	2	TCAAAGTGGAGCGCAAGCGGC
807	21	1	2	2	2	2	CAAAGTGGAGCGCAAGCGGCT
808	21	1	2	2	2	2	AAAGTGGAGCGCAAGCGGCTG
809	21	1	2	2	2	2	AAGTGGAGCGCAAGCGGCTGC
810	21	1	2	2	2	2	AGTGGAGCGCAAGCGGCTGCG
811	21	1	2	2	2	2	GTGGAGCGCAAGCGGCTGCGG
812	21	1	2	2	2	2	TGGAGCGCAAGCGGCTGCGGA
813	21	1	2	2	2	2	GGAGCGCAAGCGGCTGCGGAA
814	21	1	2	2	2	2	GAGCGCAAGCGGCTGCGGAAC
815	21	1	1	1	1	1	AGCGCAAGCGGCTGCGGAACC
816	21	1	1	1	1	1	GCGCAAGCGGCTGCGGAACCG
817	21	1	1	1	1	1	CGCAAGCGGCTGCGGAACCGG
818	21	1	1	1	1	1	GCAAGCGGCTGCGGAACCGGC
819	21	1	1	1	1	1	CAAGCGGCTGCGGAACCGGCT
820	21	1	2	2	2	2	AAGCGGCTGCGGAACCGGCTG

FIG. 20 (40)

821	21	1	2	2	2	2	AGCGGCTGCGGAACCGGCTGG
822	21	1	2	2	2	2	GCGGCTGCGGAACCGGCTGGC
823	21	1	2	2	2	2	CGGCTGCGGAACCGGCTGGCG
824	21	1	2	2	2	2	GGCTGCGGAACCGGCTGGCGG
825	21	1	2	2	2	2	GCTGCGGAACCGGCTGGCGGC
826	21	1	2	2	2	2	CTGCGGAACCGGCTGGCGGCC
827	21	1	2	2	2	2	TGCGGAACCGGCTGGCGGCCA
828	21	1	2	2	2	2	GCGGAACCGGCTGGCGGCCAC
829	21	1	2	2	2	2	CGGAACCGGCTGGCGGCCACC
830	21	1	2	2	2	2	GGAACCGGCTGGCGGCCACCA
831	21	1	2	2	2	2	GAACCGGCTGGCGGCCACCAA
832	21	1	2	2	2	2	AACCGGCTGGCGGCCACCAAG
833	21	1	2	2	2	2	ACCGGCTGGCGGCCACCAAGT
834	21	1	2	2	2	2	CCGGCTGGCGGCCACCAAGTG
835	21	1	2	2	2	2	CGGCTGGCGGCCACCAAGTGC
836	21	2	2	2	2	2	GGCTGGCGGCCACCAAGTGCC
837	21	2	2	2	2	2	GCTGGCGGCCACCAAGTGCCG
838	21	2	2	2	2	2	CTGGCGGCCACCAAGTGCCGG
839	21	2	2	2	2	2	TGGCGGCCACCAAGTGCCGGA
840	21	2	2	2	2	2	GGCGGCCACCAAGTGCCGGAA
841	21	2	2	2	2	2	GCGGCCACCAAGTGCCGGAAG

FIG. 20 (41)

842	21	2	2	2	2	2	CGGCCACCAAGTGCCGGAAGC
843	21	2	2	2	2	2	GGCCACCAAGTGCCGGAAGCG
844	21	2	2	2	2	2	GCCACCAAGTGCCGGAAGCGG
845	21	2	2	2	2	2	CCACCAAGTGCCGGAAGCGGA
846	21	2	2	2	2	2	CACCAAGTGCCGGAAGCGGAA
847	21	2	2	2	2	2	ACCAAGTGCCGGAAGCGGAAG
848	21	2	2	2	2	2	CCAAGTGCCGGAAGCGGAAGC
849	21	2	2	2	2	2	CAAGTGCCGGAAGCGGAAGCT
850	21	2	2	2	2	2	AAGTGCCGGAAGCGGAAGCTG
851	21	2	2	2	2	2	AGTGCCGGAAGCGGAAGCTGG
852	21	2	2	2	2	2	GTGCCGGAAGCGGAAGCTGGA
853	21	2	2	2	2	2	TGCCGGAAGCGGAAGCTGGAG
854	21	2	2	2	2	2	GCCGGAAGCGGAAGCTGGAGC
855	21	2	2	2	2	2	CCGGAAGCGGAAGCTGGAGCG
856	21	2	2	2	2	2	CGGAAGCGGAAGCTGGAGCGC
857	21	2	2	2	2	2	GGAAGCGGAAGCTGGAGCGCA
858	21	2	2	2	2	2	GAAGCGGAAGCTGGAGCGCAT
859	21	2	2	2	2	2	AAGCGGAAGCTGGAGCGCATC
860	21	2	2	2	2	2	AGCGGAAGCTGGAGCGCATCG
861	21	2	2	2	2	2	GCGGAAGCTGGAGCGCATCGC
862	21	2	2	2	2	2	CGGAAGCTGGAGCGCATCGCG

FIG. 20 (42)

863	21	2	2	2	2	2	GGAAGCTGGAGCGCATCGCGC
864	21	2	2	2	2	2	GAAGCTGGAGCGCATCGCGCG
865	21	2	2	2	2	2	AAGCTGGAGCGCATCGCGCGC
866	21	2	2	2	2	2	AGCTGGAGCGCATCGCGCGCC
867	21	2	2	2	2	2	GCTGGAGCGCATCGCGCGCCT
868	21	2	2	2	2	2	CTGGAGCGCATCGCGCGCCTG
869	21	2	2	2	2	2	TGGAGCGCATCGCGCGCCTGG
870	21	2	2	2	2	2	GGAGCGCATCGCGCGCCTGGA
871	21	2	2	2	2	2	GAGCGCATCGCGCGCCTGGAG
872	21	2	2	2	2	2	AGCGCATCGCGCGCCTGGAGG
873	21	2	2	2	2	2	GCGCATCGCGCGCCTGGAGGA
874	21	2	2	2	2	2	CGCATCGCGCGCCTGGAGGAC
875	21	2	2	2	2	2	GCATCGCGCGCCTGGAGGACA
876	21	2	2	2	2	2	CATCGCGCGCCTGGAGGACAA
877	21	2	2	2	2	2	ATCGCGCGCCTGGAGGACAAG
878	21	2	2	2	2	2	TCGCGCGCCTGGAGGACAAGG
879	21	2	2	2	2	2	CGCGCGCCTGGAGGACAAGGT
880	21	2	2	2	2	2	GCGCGCCTGGAGGACAAGGTG
881	21	2	2	2	2	2	CGCGCCTGGAGGACAAGGTGA
882	21	2	2	2	2	2	GCGCCTGGAGGACAAGGTGAA
883	21	2	2	2	2	2	CGCCTGGAGGACAAGGTGAAG
884	21	2	2	2	2	2	GCCTGGAGGACAAGGTGAAGA

FIG. 20 (43)

885	21	2	2	2	2	2	CCTGGAGGACAAGGTGAAGAC
886	21	1	2	2	2	2	CTGGAGGACAAGGTGAAGACG
887	21	1	2	2	2	2	TGGAGGACAAGGTGAAGACGC
888	21	1	2	2	2	2	GGAGGACAAGGTGAAGACGCT
889	21	1	2	2	2	2	GAGGACAAGGTGAAGACGCTC
890	21	1	2	2	2	2	AGGACAAGGTGAAGACGCTCA
891	21	1	2	2	2	2	GGACAAGGTGAAGACGCTCAA
892	21	1	2	2	2	2	GACAAGGTGAAGACGCTCAAG
893	21	1	2	2	2	2	ACAAGGTGAAGACGCTCAAGG
894	21	1	2	2	2	2	CAAGGTGAAGACGCTCAAGGC
895	21	1	1	1	1	1	AAGGTGAAGACGCTCAAGGCC
896	21	1	1	1	1	1	AGGTGAAGACGCTCAAGGCCG
897	21	1	1	1	1	1	GGTGAAGACGCTCAAGGCCGA
898	21	1	1	1	1	1	GTGAAGACGCTCAAGGCCGAG
899	21	1	1	1	1	1	TGAAGACGCTCAAGGCCGAGA
900	21	1	1	1	1	1	GAAGACGCTCAAGGCCGAGAA
901	21	1	1	1	1	1	AAGACGCTCAAGGCCGAGAAC
902	21	1	1	1	1	1	AGACGCTCAAGGCCGAGAACG
903	21	1	1	1	1	1	GACGCTCAAGGCCGAGAACGC
904	21	1	1	1	1	1	ACGCTCAAGGCCGAGAACGCG
905	21	1	1	1	1	1	CGCTCAAGGCCGAGAACGCGG

FIG. 20 (44)

906	21	1	1	1	1	1	GCTCAAGGCCGAGAACGCGGG
907	21	1	2	2	2	2	CTCAAGGCCGAGAACGCGGGG
908	21	1	2	2	2	2	TCAAGGCCGAGAACGCGGGGC
909	21	1	2	2	2	2	CAAGGCCGAGAACGCGGGGCT
910	21	1	2	2	2	2	AAGGCCGAGAACGCGGGGCTG
911	21	1	2	2	2	2	AGGCCGAGAACGCGGGGCTGT
912	21	1	2	2	2	2	GGCCGAGAACGCGGGGCTGTC
913	21	1	2	2	2	2	GCCGAGAACGCGGGGCTGTCG
914	21	1	2	2	2	2	CCGAGAACGCGGGGCTGTCGA
915	21	1	2	2	2	2	CGAGAACGCGGGGCTGTCGAG
916	21	2	2	2	2	2	GAGAACGCGGGGCTGTCGAGT
917	21	1	2	2	2	2	AGAACGCGGGGCTGTCGAGTA
918	21	1	2	2	2	2	GAACGCGGGGCTGTCGAGTAC
919	21	1	1	1	1	1	AACGCGGGGCTGTCGAGTACC
920	21	1	1	1	1	1	ACGCGGGGCTGTCGAGTACCG
921	21	1	1	1	1	1	CGCGGGGCTGTCGAGTACCGC
922	21	1	1	1	1	1	GCGGGGCTGTCGAGTACCGCC
923	21	1	1	1	1	1	CGGGGCTGTCGAGTACCGCCG
924	21	1	1	1	1	1	GGGGCTGTCGAGTACCGCCGG
925	21	1	1	1	1	1	GGGCTGTCGAGTACCGCCGGC
926	21	1	1	1	1	1	GGCTGTCGAGTACCGCCGGCC

FIG. 20 (45)

927	21	1	1	1	1	1	GCTGTCGAGTACCGCCGGCCT
928	21	1	1	1	1	1	CTGTCGAGTACCGCCGGCCTC
929	21	1	1	1	1	1	TGTCGAGTACCGCCGGCCTCC
930	21	1	1	1	1	1	GTCGAGTACCGCCGGCCTCCT
931	21	1	1	1	1	1	TCGAGTACCGCCGGCCTCCTC
932	21	1	1	1	1	1	CGAGTACCGCCGGCCTCCTCC
933	21	1	1	1	1	1	GAGTACCGCCGGCCTCCTCCG
934	21	1	1	1	1	1	AGTACCGCCGGCCTCCTCCGG
935	21	1	1	1	1	1	GTACCGCCGGCCTCCTCCGGG
936	21	1	1	1	1	1	TACCGCCGGCCTCCTCCGGGA
937	21	1	1	1	1	1	ACCGCCGGCCTCCTCCGGGAG
938	21	1	1	1	1	1	CCGCCGGCCTCCTCCGGGAGC
939	21	1	1	1	1	1	CGCCGGCCTCCTCCGGGAGCA
940	21	1	1	1	1	1	GCCGGCCTCCTCCGGGAGCAG
941	21	1	1	1	1	1	CCGGCCTCCTCCGGGAGCAGG
942	21	1	1	1	1	1	CGGCCTCCTCCGGGAGCAGGT
943	21	1	1	1	1	1	GGCCTCCTCCGGGAGCAGGTG
944	21	1	1	1	1	1	GCCTCCTCCGGGAGCAGGTGG
945	21	1	1	1	1	1	CCTCCTCCGGGAGCAGGTGGC
946	21	1	1	1	1	1	CTCCTCCGGGAGCAGGTGGCC
947	21	1	1	1	1	1	TCCTCCGGGAGCAGGTGGCCC
948	21	1	1	1	1	1	CCTCCGGGAGCAGGTGGCCCA

FIG. 20 (46)

949	21	1	1	1	1	1	CTCCGGGAGCAGGTGGCCCAG
950	21	1	1	1	1	1	TCCGGGAGCAGGTGGCCCAGC
951	21	1	1	1	1	1	CCGGGAGCAGGTGGCCCAGCT
952	21	1	1	1	1	1	CGGGAGCAGGTGGCCCAGCTC
953	21	1	1	1	1	1	GGGAGCAGGTGGCCCAGCTCA
954	21	1	1	1	1	1	GGAGCAGGTGGCCCAGCTCAA
955	21	1	2	2	2	2	GAGCAGGTGGCCCAGCTCAAA
956	21	1	2	2	2	2	AGCAGGTGGCCCAGCTCAAAC
957	21	1	2	2	2	2	GCAGGTGGCCCAGCTCAAACA
958	21	1	2	2	2	2	CAGGTGGCCCAGCTCAAACAG
959	21	1	2	2	2	2	AGGTGGCCCAGCTCAAACAGA
960	21	1	2	2	2	2	GGTGGCCCAGCTCAAACAGAA
961	21	1	1	1	1	1	GTGGCCCAGCTCAAACAGAAG
962	21	1	1	1	1	1	TGGCCCAGCTCAAACAGAAGG
963	21	1	1	1	1	1	GGCCCAGCTCAAACAGAAGGT
964	21	1	1	1	1	1	GCCCAGCTCAAACAGAAGGTC
965	21	1	1	1	1	1	CCCAGCTCAAACAGAAGGTCA
966	21	1	1	1	1	1	CCAGCTCAAACAGAAGGTCAT
967	21	1	2	2	2	2	CAGCTCAAACAGAAGGTCATG
968	21	1	2	2	2	2	AGCTCAAACAGAAGGTCATGA
969	21	1	2	2	2	2	GCTCAAACAGAAGGTCATGAC

FIG. 20 (47)

970	21	1	2	2	2	2	CTCAAACAGAAGGTCATGACC
971	21	1	2	2	2	2	TCAAACAGAAGGTCATGACCC
972	21	1	2	2	2	2	CAAACAGAAGGTCATGACCCA
973	21	1	1	1	1	1	AAACAGAAGGTCATGACCCAC
974	21	1	1	1	1	1	AACAGAAGGTCATGACCCACG
975	21	1	1	1	1	1	ACAGAAGGTCATGACCCACGT
976	21	1	2	2	2	2	CAGAAGGTCATGACCCACGTC
977	21	1	2	2	2	2	AGAAGGTCATGACCCACGTCA
978	21	1	2	2	2	2	GAAGGTCATGACCCACGTCAG
979	21	1	2	2	2	2	AAGGTCATGACCCACGTCAGC
980	21	1	2	2	2	2	AGGTCATGACCCACGTCAGCA
981	21	1	2	2	2	2	GGTCATGACCCACGTCAGCAA
982	21	1	2	2	2	2	GTCATGACCCACGTCAGCAAC
983	21	1	2	2	2	2	TCATGACCCACGTCAGCAACG
984	21	1	2	2	2	2	CATGACCCACGTCAGCAACGG
985	21	1	2	2	2	2	ATGACCCACGTCAGCAACGGC
986	21	1	2	2	2	2	TGACCCACGTCAGCAACGGCT
987	21	1	2	2	2	2	GACCCACGTCAGCAACGGCTG
988	21	1	1	1	1	1	ACCCACGTCAGCAACGGCTGT
989	21	1	1	1	1	1	CCCACGTCAGCAACGGCTGTC
990	21	1	1	1	1	1	CCACGTCAGCAACGGCTGTCA

FIG. 20 (48)

991	21	1	1	1	1	1	CACGTCAGCAACGGCTGTCAG
992	21	1	1	1	1	1	ACGTCAGCAACGGCTGTCAGC
993	21	1	1	1	1	1	CGTCAGCAACGGCTGTCAGCT
994	21	1	1	1	1	1	GTCAGCAACGGCTGTCAGCTG
995	21	1	1	1	1	1	TCAGCAACGGCTGTCAGCTGC
996	21	1	1	1	1	1	CAGCAACGGCTGTCAGCTGCT
997	21	1	1	1	1	1	AGCAACGGCTGTCAGCTGCTG
998	21	1	1	1	1	1	GCAACGGCTGTCAGCTGCTGC
999	21	1	1	1	1	1	CAACGGCTGTCAGCTGCTGCT
1000	21	1	1	1	1	1	AACGGCTGTCAGCTGCTGCTT
1001	21	1	1	1	1	1	ACGGCTGTCAGCTGCTGCTTG
1002	21	1	1	1	1	1	CGGCTGTCAGCTGCTGCTTGG
1003	21	1	1	1	1	1	GGCTGTCAGCTGCTGCTTGGG
1004	21	1	1	1	1	1	GCTGTCAGCTGCTGCTTGGGG
1005	21	1	1	1	1	1	CTGTCAGCTGCTGCTTGGGGT
1006	21	1	1	1	1	1	TGTCAGCTGCTGCTTGGGGTC
1007	21	1	1	1	1	1	GTCAGCTGCTGCTTGGGGTCA
1008	21	1	1	1	1	1	TCAGCTGCTGCTTGGGGTCAA
1009	21	1	1	1	1	1	CAGCTGCTGCTTGGGGTCAAG
1010	21	1	1	1	1	1	AGCTGCTGCTTGGGGTCAAGG
1011	21	1	1	1	1	1	GCTGCTGCTTGGGGTCAAGGG
1012	21	1	1	1	1	1	CTGCTGCTTGGGGTCAAGGGA

FIG. 20 (49)

1013	21	1	2	2	2	2	TGCTGCTTGGGGTCAAGGGAC
1014	21	1	2	2	2	2	GCTGCTTGGGGTCAAGGGACA
1015	21	1	2	2	2	2	CTGCTTGGGGTCAAGGGACAC
1016	21	1	2	2	2	2	TGCTTGGGGTCAAGGGACACG
1017	21	1	2	2	2	2	GCTTGGGGTCAAGGGACACGC
1018	21	1	2	2	2	2	CTTGGGGTCAAGGGACACGCC
1019	21	1	2	2	2	2	TTGGGGTCAAGGGACACGCCT
1020	21	1	2	2	2	2	TGGGGTCAAGGGACACGCCTT
1021	21	2	2	2	2	2	GGGGTCAAGGGACACGCCTTC
1022	21	2	2	2	2	2	GGGTCAAGGGACACGCCTTCT
1023	21	2	2	2	2	2	GGTCAAGGGACACGCCTTCTG
1024	21	2	2	2	2	2	GTCAAGGGACACGCCTTCTGA

FIG. 21

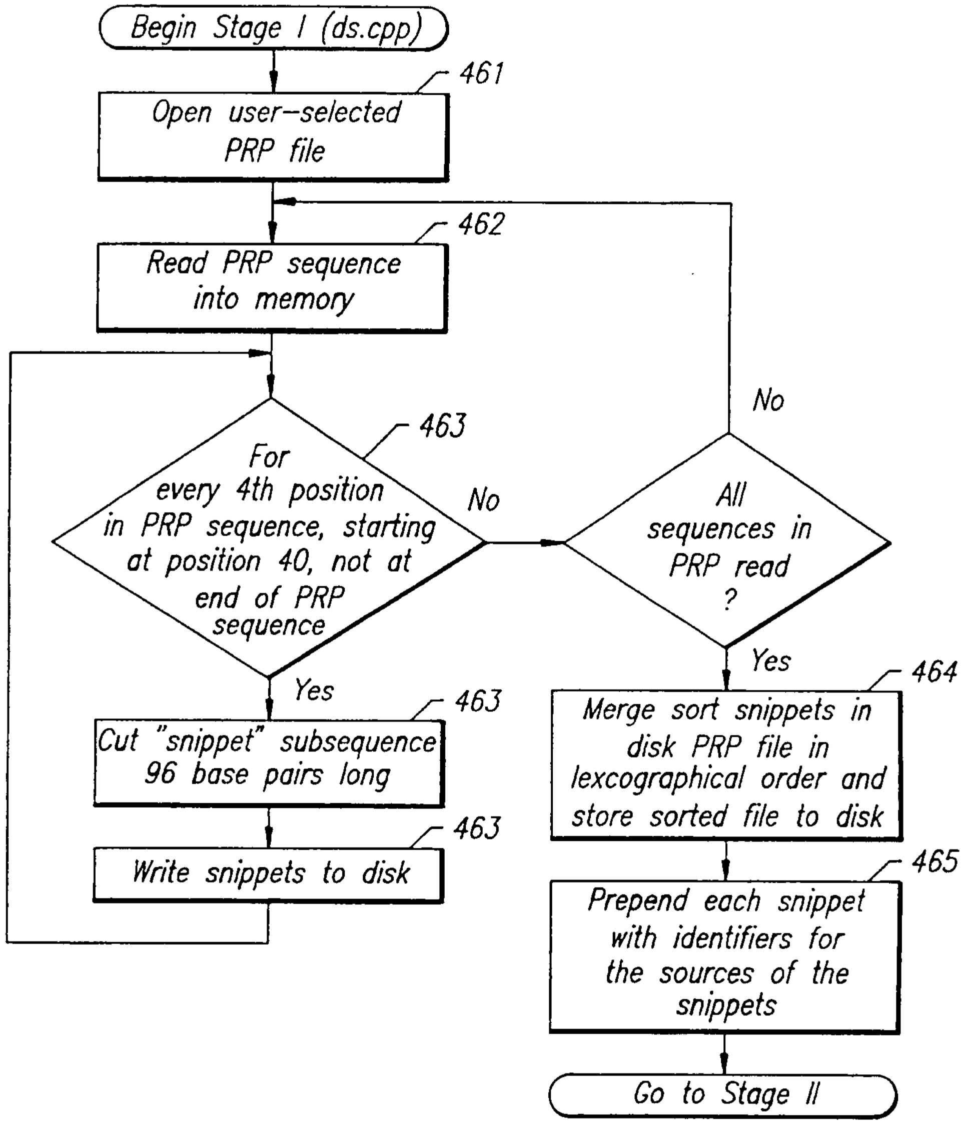

Begin Stage I (ds.cpp)
461
Open user-selected PRP file
462
Read PRP sequence into memory
463
For every 4th position in PRP sequence, starting at position 40, not at end of PRP sequence
No
All sequences in PRP read ?
No
Yes
463
Cut "snippet" subsequence 96 base pairs long
463
Write snippets to disk
Yes
464
Merge sort snippets in disk PRP file in lexcographical order and store sorted file to disk
465
Prepend each snippet with identifiers for the sources of the snippets
Go to Stage II

FIG. 22

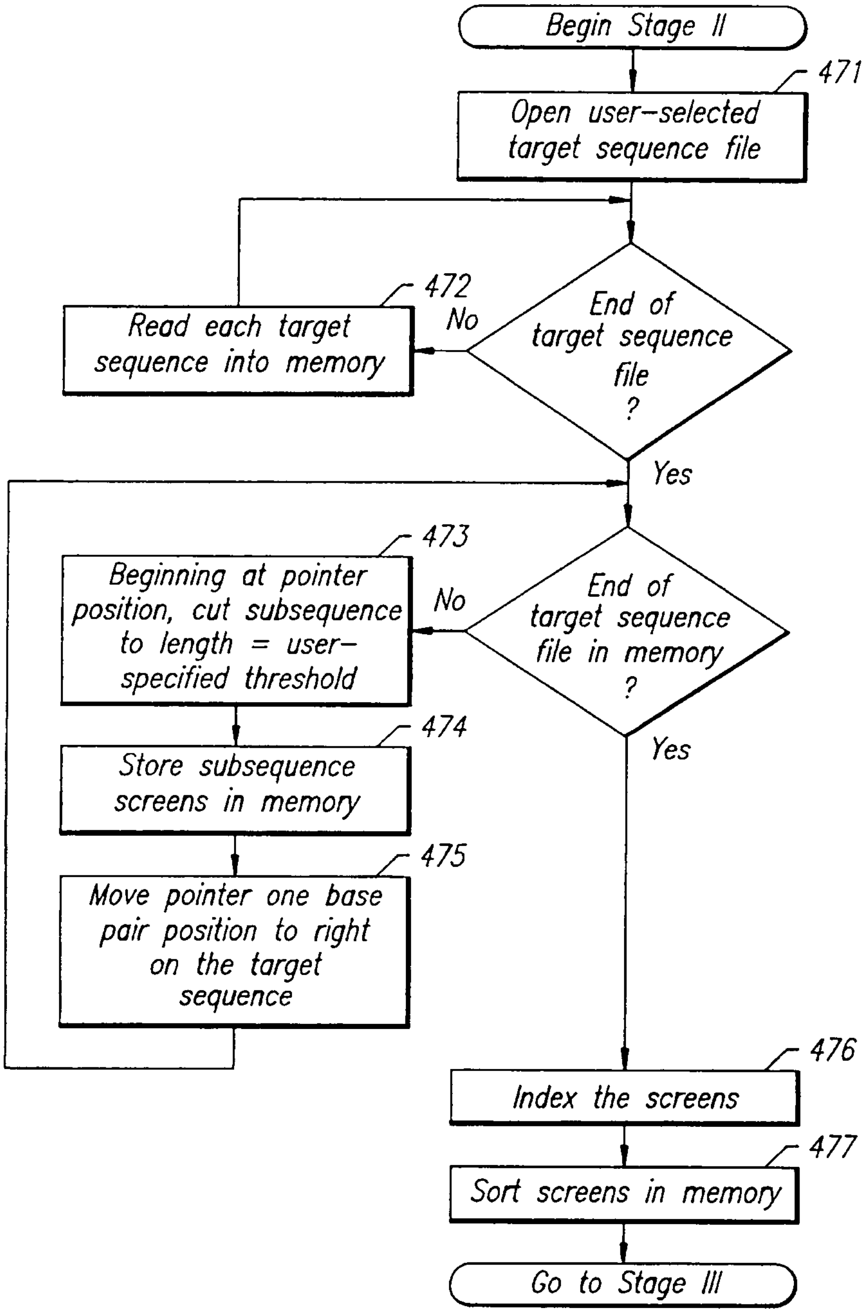
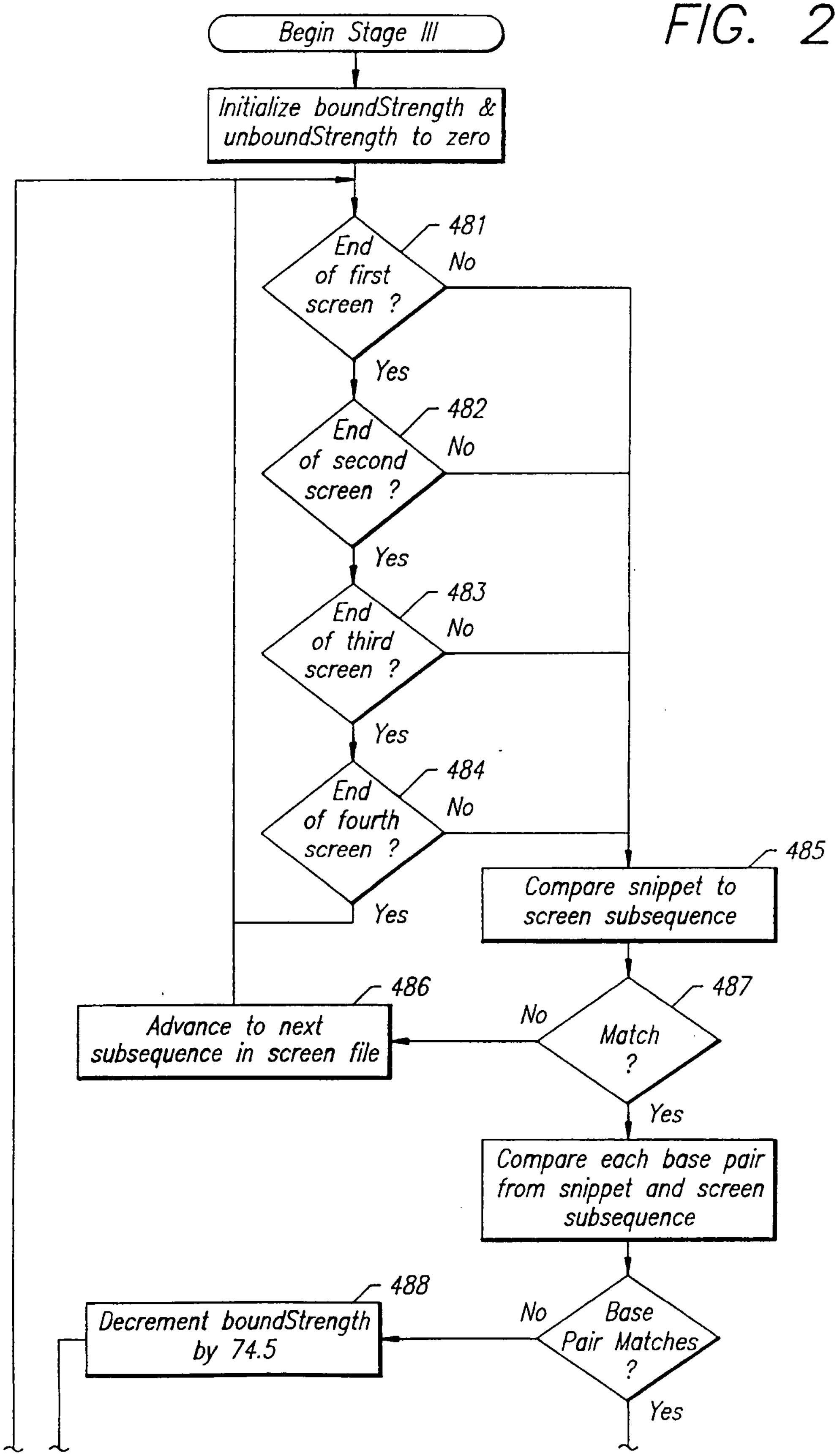

Begin Stage II
471
Open user-selected target sequence file
End of target sequence file ?
No
472
Read each target sequence into memory
Yes
End of target sequence file in memory ?
No
473
Beginning at pointer position, cut subsequence to length = user-specified threshold
474
Store subsequence screens in memory
475
Move pointer one base pair position to right on the target sequence
Yes
476
Index the screens
477
Sort screens in memory
Go to Stage III

FIG. 23(1)


Begin Stage III
Initialize boundStrength & unboundStrength to zero
481
End of first screen ?
No
Yes
482
End of second screen ?
No
Yes
483
End of third screen ?
No
Yes
484
End of fourth screen ?
No
Yes
485
Compare snippet to screen subsequence
486
Advance to next subsequence in screen file
487
Match ?
No
Yes
Compare each base pair from snippet and screen subsequence
488
Decrement boundStrength by 74.5
Base Pair Matches ?
No
Yes

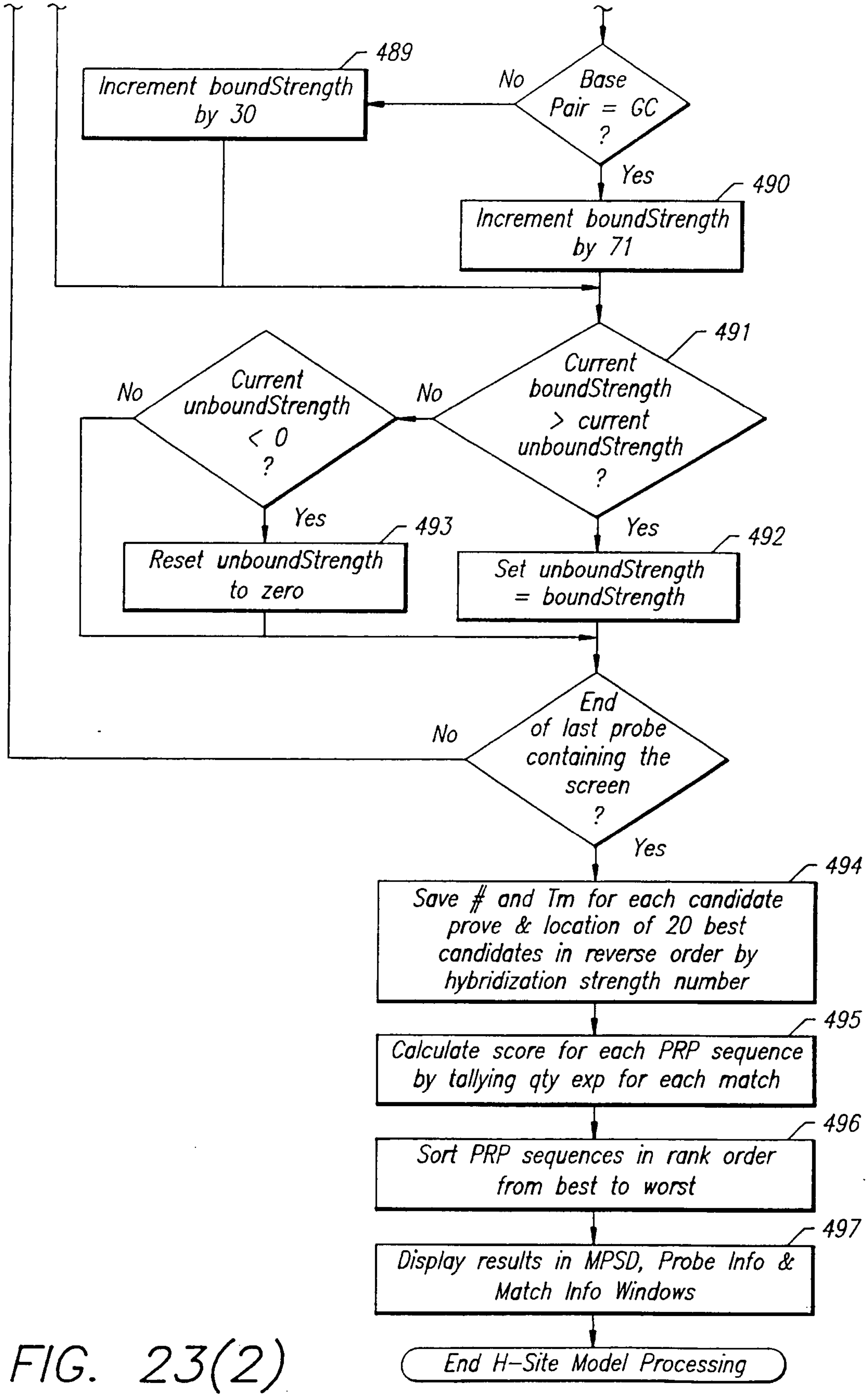

489
Increment boundStrength by 30
No
Base Pair = GC ?
Yes
490
Increment boundStrength by 71
491
No
Current unboundStrength < 0 ?
No
Current boundStrength > current unboundStrength ?
Yes
493
Reset unboundStrength to zero
Yes
492
Set unboundStrength = boundStrength
No
End of last probe containing the screen ?
Yes
494
Save # and Tm for each candidate prove & location of 20 best candidates in reverse order by hybridization strength number
495
Calculate score for each PRP sequence by tallying qty exp for each match
496
Sort PRP sequences in rank order from best to worst
497
Display results in MPSD, Probe Info & Match Info Windows
End H-Site Model Processing

FIG. 23(2)

FIG. 24A (1)

```
OligoProbe DesignStation

Probes:   C:\HITACHI\HUMBJUNX.CDS
Datatbase:   C:\HITACHI\JUNMIX.SEQ

Mismatch Model, l = 21, k = 4

 Position    Mismatches                                         screensN
   length    0     1     2     3     4     5     6     7     8        Probe

     1 21    0     0     0     0     0   ATGTGCACTAAAATGGAACAG
     2 21    0     0     0     0     0   TGTGCACTAAAATGGAACAGC
     3 21    0     0     0     0     0   GTGCACTAAAATGGAACAGCC
     4 21    0     0     0     0     0   TGCACTAAAATGGAACAGCCC
     5 21    0     0     0     0     0   GCACTAAAATGGAACAGCCCT
     6 21    0     0     0     0     0   CACTAAAATGGAACAGCCCTT
     7 21    0     0     0     0     0   ACTAAAATGGAACAGCCCTTC
     8 21    0     0     0     0     0   CTAAAATGGAACAGCCCTTCT
     9 21    0     0     0     0     0   TAAAATGGAACAGCCCTTCTA
    10 21    0     0     0     0     0   AAAATGGAACAGCCCTTCTAC
```

FIG. 24A (2)

11	21	0	0	0	0	0	AAATGGAACAGCCCTTCTACC
12	21	0	0	0	0	0	AATGGAACAGCCCTTCTACCA
13	21	0	0	0	0	0	ATGGAACAGCCCTTCTACCAC
14	21	0	0	0	0	0	TGGAACAGCCCTTCTACCACG
15	21	0	0	0	0	0	GGAACAGCCCTTCTACCACGA
16	21	0	0	0	0	0	GAACAGCCCTTCTACCACGAC
17	21	0	0	0	0	0	AACAGCCCTTCTACCACGACG
18	21	0	0	0	0	0	ACAGCCCTTCTACCACGACGA
19	21	0	0	0	0	0	CAGCCCTTCTACCACGACGAC
20	21	0	0	0	0	0	AGCCCTTCTACCACGACGACT
21	21	0	0	0	0	0	GCCCTTCTACCACGACGACTC
22	21	0	0	0	0	0	CCCTTCTACCACGACGACTCA
23	21	0	0	0	0	0	CCTTCTACCACGACGACTCAT
24	21	0	0	0	0	0	CTTCTACCACGACGACTCATA
25	21	0	0	0	0	0	TTCTACCACGACGACTCATAC
26	21	0	0	0	0	0	TCTACCACGACGACTCATACA
27	21	0	0	0	0	0	CTACCACGACGACTCATACAC
28	21	0	0	0	0	0	TACCACGACGACTCATACACA
29	21	0	0	0	0	0	ACCACGACGACTCATACACAG
30	21	0	0	0	0	0	CCACGACGACTCATACACAGC
31	21	0	0	0	0	0	CACGACGACTCATACACAGCT

FIG. 24A (3)

32	21	0	0	0	0	0	ACGACGACTCATACACAGCTA
33	21	0	0	0	0	0	CGACGACTCATACACAGCTAC
34	21	0	0	0	0	0	GACGACTCATACACAGCTACG
35	21	0	0	0	0	0	ACGACTCATACACAGCTACGG
36	21	0	0	0	0	0	CGACTCATACACAGCTACGGG
37	21	0	0	0	0	0	GACTCATACACAGCTACGGGA
38	21	0	0	0	0	0	ACTCATACACAGCTACGGGAT
39	21	0	0	0	0	0	CTCATACACAGCTACGGGATA
40	21	0	0	0	0	0	TCATACACAGCTACGGGATAC
41	21	0	0	0	0	0	CATACACAGCTACGGGATACG
42	21	0	0	0	0	0	ATACACAGCTACGGGATACGG
43	21	0	0	0	0	0	TACACAGCTACGGGATACGGC
44	21	0	0	0	0	0	ACACAGCTACGGGATACGGCC
45	21	0	0	0	0	0	CACAGCTACGGGATACGGCCG
46	21	0	0	0	0	0	ACAGCTACGGGATACGGCCGG
47	21	0	0	0	0	0	CAGCTACGGGATACGGCCGGG
48	21	0	0	0	0	0	AGCTACGGGATACGGCCGGGC
49	21	0	0	0	0	0	GCTACGGGATACGGCCGGGCC
50	21	0	0	0	0	0	CTACGGGATACGGCCGGGCCC
51	21	0	0	0	0	0	TACGGGATACGGCCGGGCCCC
52	21	0	0	0	0	0	ACGGGATACGGCCGGGCCCCT
53	21	0	0	0	0	0	CGGGATACGGCCGGGCCCCTG

FIG. 24A (4)

54	21	0	0	0	0	0	GGGATACGGCCGGGCCCCTGG
55	21	0	0	0	0	0	GGATACGGCCGGGCCCCTGGT
56	21	0	0	0	0	0	GATACGGCCGGGCCCCTGGTG
57	21	0	0	0	0	0	ATACGGCCGGGCCCCTGGTGG
58	21	0	0	0	0	0	TACGGCCGGGCCCCTGGTGGC
59	21	0	0	0	0	0	ACGGCCGGGCCCCTGGTGGCC
60	21	0	0	0	0	0	CGGCCGGGCCCCTGGTGGCCT
61	21	0	0	0	0	0	GGCCGGGCCCCTGGTGGCCTC
62	21	0	0	0	0	0	GCCGGGCCCCTGGTGGCCTCT
63	21	0	0	0	0	0	CCGGGCCCCTGGTGGCCTCTC
64	21	0	0	0	0	0	CGGGCCCCTGGTGGCCTCTCT
65	21	0	0	0	0	0	GGGCCCCTGGTGGCCTCTCTC
66	21	0	0	0	0	0	GGCCCCTGGTGGCCTCTCTCT
67	21	0	0	0	0	0	GCCCCTGGTGGCCTCTCTCTA
68	21	0	0	0	0	0	CCCCTGGTGGCCTCTCTCTAC
69	21	0	0	0	0	0	CCCTGGTGGCCTCTCTCTACA
70	21	0	0	0	0	0	CCTGGTGGCCTCTCTCTACAC
71	21	0	0	0	0	0	CTGGTGGCCTCTCTCTACACG
72	21	0	0	0	0	0	TGGTGGCCTCTCTCTACACGA
73	21	0	0	0	0	0	GGTGGCCTCTCTCTACACGAC
74	21	0	0	0	0	0	GTGGCCTCTCTCTACACGACT

FIG. 24A (5)

75	21	0	0	0	0	0	TGGCCTCTCTCTACACGACTA
76	21	0	0	0	0	0	GGCCTCTCTCTACACGACTAC
77	21	0	0	0	0	0	GCCTCTCTCTACACGACTACA
78	21	0	0	0	0	0	CCTCTCTCTACACGACTACAA
79	21	0	0	0	0	0	CTCTCTCTACACGACTACAAA
80	21	0	0	0	0	0	TCTCTCTACACGACTACAAAC
81	21	0	0	0	0	0	CTCTCTACACGACTACAAACT
82	21	0	0	0	0	0	TCTCTACACGACTACAAACTC
83	21	0	0	0	0	0	CTCTACACGACTACAAACTCC
84	21	0	0	0	0	0	TCTACACGACTACAAACTCCT
85	21	0	0	0	0	0	CTACACGACTACAAACTCCTG
86	21	0	0	0	0	0	TACACGACTACAAACTCCTGA
87	21	0	0	0	0	0	ACACGACTACAAACTCCTGAA
88	21	0	0	0	0	0	CACGACTACAAACTCCTGAAA
89	21	0	0	0	0	0	ACGACTACAAACTCCTGAAAC
90	21	0	0	0	0	0	CGACTACAAACTCCTGAAACC
91	21	0	0	0	0	0	GACTACAAACTCCTGAAACCG
92	21	0	0	0	0	0	ACTACAAACTCCTGAAACCGA
93	21	0	0	0	0	0	CTACAAACTCCTGAAACCGAG
94	21	0	0	0	0	0	TACAAACTCCTGAAACCGAGC
95	21	0	0	0	0	0	ACAAACTCCTGAAACCGAGCC

FIG. 24A (6)

96	21	0	0	0	0	0	CAAACTCCTGAAACCGAGCCT
97	21	0	0	0	0	0	AAACTCCTGAAACCGAGCCTG
98	21	0	0	0	0	0	AACTCCTGAAACCGAGCCTGG
99	21	0	0	0	0	0	ACTCCTGAAACCGAGCCTGGC
100	21	0	0	0	0	0	CTCCTGAAACCGAGCCTGGCG
101	21	0	0	0	0	0	TCCTGAAACCGAGCCTGGCGG
102	21	0	0	0	0	0	CCTGAAACCGAGCCTGGCGGT
103	21	0	0	0	0	0	CTGAAACCGAGCCTGGCGGTC
104	21	0	0	0	0	0	TGAAACCGAGCCTGGCGGTCA
105	21	0	0	0	0	0	GAAACCGAGCCTGGCGGTCAA
106	21	0	0	0	0	0	AAACCGAGCCTGGCGGTCAAC
107	21	0	0	0	0	0	AACCGAGCCTGGCGGTCAACC
108	21	0	0	0	0	0	ACCGAGCCTGGCGGTCAACCT
109	21	0	0	0	0	0	CCGAGCCTGGCGGTCAACCTG
110	21	0	0	0	0	0	CGAGCCTGGCGGTCAACCTGG
111	21	0	0	0	0	0	GAGCCTGGCGGTCAACCTGGC
112	21	0	0	0	0	0	AGCCTGGCGGTCAACCTGGCC
113	21	0	0	0	0	0	GCCTGGCGGTCAACCTGGCCG
114	21	0	0	0	0	0	CCTGGCGGTCAACCTGGCCGA
115	21	0	0	0	0	0	CTGGCGGTCAACCTGGCCGAC

FIG. 24A (7)

116	21	0	0	0	0	0	TGGCGGTCAACCTGGCCGACC
117	21	0	0	0	0	0	GGCGGTCAACCTGGCCGACCC
118	21	0	0	0	0	0	GCGGTCAACCTGGCCGACCCC
119	21	0	0	0	0	0	CGGTCAACCTGGCCGACCCCT
120	21	0	0	0	0	0	GGTCAACCTGGCCGACCCCTA
121	21	0	0	0	0	0	GTCAACCTGGCCGACCCCTAC
122	21	0	0	0	0	0	TCAACCTGGCCGACCCCTACC
123	21	0	0	0	0	0	CAACCTGGCCGACCCCTACCG
124	21	0	0	0	0	0	AACCTGGCCGACCCCTACCGG
125	21	0	0	0	0	0	ACCTGGCCGACCCCTACCGGA
126	21	0	0	0	0	0	CCTGGCCGACCCCTACCGGAG
127	21	0	0	0	0	0	CTGGCCGACCCCTACCGGAGT
128	21	0	0	0	0	0	TGGCCGACCCCTACCGGAGTC
129	21	0	0	0	0	0	GGCCGACCCCTACCGGAGTCT
130	21	0	0	0	0	0	GCCGACCCCTACCGGAGTCTC
131	21	0	0	0	0	0	CCGACCCCTACCGGAGTCTCA
132	21	0	0	0	0	0	CGACCCCTACCGGAGTCTCAA
133	21	0	0	0	0	0	GACCCCTACCGGAGTCTCAAA
134	21	0	0	0	0	0	ACCCCTACCGGAGTCTCAAAG
135	21	0	0	0	0	0	CCCCTACCGGAGTCTCAAAGC
136	21	0	0	0	0	0	CCCTACCGGAGTCTCAAAGCG

FIG. 24A (8)

137	21	0	0	0	0	0	CCTACCGGAGTCTCAAAGCGC
138	21	0	0	0	0	0	CTACCGGAGTCTCAAAGCGCC
139	21	0	0	0	0	0	TACCGGAGTCTCAAAGCGCCT
140	21	0	0	0	0	0	ACCGGAGTCTCAAAGCGCCTG
141	21	0	0	0	0	0	CCGGAGTCTCAAAGCGCCTGG
142	21	0	0	0	0	0	CGGAGTCTCAAAGCGCCTGGG
143	21	0	0	0	0	0	GGAGTCTCAAAGCGCCTGGGG
144	21	0	0	0	0	0	GAGTCTCAAAGCGCCTGGGGC
145	21	0	0	0	0	0	AGTCTCAAAGCGCCTGGGGCT
146	21	0	0	0	0	0	GTCTCAAAGCGCCTGGGGCTC
147	21	0	0	0	0	0	TCTCAAAGCGCCTGGGGCTCG
148	21	0	0	0	0	0	CTCAAAGCGCCTGGGGCTCGC
149	21	0	0	0	0	0	TCAAAGCGCCTGGGGCTCGCG
150	21	0	0	0	0	0	CAAAGCGCCTGGGGCTCGCGG
151	21	0	0	0	0	0	AAAGCGCCTGGGGCTCGCGGA
152	21	0	0	0	0	0	AAGCGCCTGGGGCTCGCGGAC
153	21	0	0	0	0	0	AGCGCCTGGGGCTCGCGGACC
154	21	0	0	0	0	0	GCGCCTGGGGCTCGCGGACCC
155	21	0	0	0	0	0	CGCCTGGGGCTCGCGGACCCG
156	21	0	0	0	0	0	GCCTGGGGCTCGCGGACCCGG
157	21	0	0	0	0	0	CCTGGGGCTCGCGGACCCGGC

FIG. 24A (9)

158	21	0	0	0	0	0	CTGGGGCTCGCGGACCCGGCC
159	21	0	0	0	0	0	TGGGGCTCGCGGACCCGGCCC
160	21	0	0	0	0	0	GGGGCTCGCGGACCCGGCCCA
161	21	0	0	0	0	0	GGGCTCGCGGACCCGGCCCAG
162	21	0	0	0	0	0	GGCTCGCGGACCCGGCCCAGA
163	21	0	0	0	0	0	GCTCGCGGACCCGGCCCAGAG
164	21	0	0	0	0	0	CTCGCGGACCCGGCCCAGAGG
165	21	0	0	0	0	0	TCGCGGACCCGGCCCAGAGGG
166	21	0	0	0	0	0	CGCGGACCCGGCCCAGAGGGC
167	21	0	0	0	0	0	GCGGACCCGGCCCAGAGGGCG
168	21	0	0	0	0	0	CGGACCCGGCCCAGAGGGCGG
169	21	0	0	0	0	0	GGACCCGGCCCAGAGGGCGGC
170	21	0	0	0	0	0	GACCCGGCCCAGAGGGCGGCG
171	21	0	0	0	0	0	ACCCGGCCCAGAGGGCGGCGG
172	21	0	0	0	0	0	CCCGGCCCAGAGGGCGGCGGT
173	21	0	0	0	0	0	CCGGCCCAGAGGGCGGCGGTG
174	21	0	0	0	0	0	CGGCCCAGAGGGCGGCGGTGG
175	21	0	0	0	0	0	GGCCCAGAGGGCGGCGGTGGC
176	21	0	0	0	0	0	GCCCAGAGGGCGGCGGTGGCG
177	21	0	0	0	0	0	CCCAGAGGGCGGCGGTGGCGG
178	21	0	0	0	0	0	CCAGAGGGCGGCGGTGGCGGC

FIG. 24A (10)

179	21	0	0	0	0	0	CAGAGGGCGGCGGTGGCGGCA
180	21	0	0	0	0	0	AGAGGGCGGCGGTGGCGGCAG
181	21	0	0	0	0	0	GAGGGCGGCGGTGGCGGCAGC
182	21	0	0	0	0	0	AGGGCGGCGGTGGCGGCAGCT
183	21	0	0	0	0	0	GGGCGGCGGTGGCGGCAGCTA
184	21	0	0	0	0	0	GGCGGCGGTGGCGGCAGCTAC
185	21	0	0	0	0	0	GCGGCGGTGGCGGCAGCTACT
186	21	0	0	0	0	0	CGGCGGTGGCGGCAGCTACTT
187	21	0	0	0	0	0	GGCGGTGGCGGCAGCTACTTT
188	21	0	0	0	0	0	GCGGTGGCGGCAGCTACTTTT
189	21	0	0	0	0	0	CGGTGGCGGCAGCTACTTTTC
190	21	0	0	0	0	0	GGTGGCGGCAGCTACTTTTCT
191	21	0	0	0	0	0	GTGGCGGCAGCTACTTTTCTG
192	21	0	0	0	0	0	TGGCGGCAGCTACTTTTCTGG
193	21	0	0	0	0	0	GGCGGCAGCTACTTTTCTGGT
194	21	0	0	0	0	0	GCGGCAGCTACTTTTCTGGTC
195	21	0	0	0	0	0	CGGCAGCTACTTTTCTGGTCA
196	21	0	0	0	0	0	GGCAGCTACTTTTCTGGTCAG
197	21	0	0	0	0	0	GCAGCTACTTTTCTGGTCAGG
198	21	0	0	0	0	0	CAGCTACTTTTCTGGTCAGGG
199	21	0	0	0	0	0	AGCTACTTTTCTGGTCAGGGC

FIG. 24A (11)

200	21	0	0	0	0	0	GCTACTTTTCTGGTCAGGGCT
201	21	0	0	0	0	0	CTACTTTTCTGGTCAGGGCTC
202	21	0	0	0	0	0	TACTTTTCTGGTCAGGGCTCG
203	21	0	0	0	0	0	ACTTTTCTGGTCAGGGCTCGG
204	21	0	0	0	0	0	CTTTTCTGGTCAGGGCTCGGA
205	21	0	0	0	0	0	TTTTCTGGTCAGGGCTCGGAC
206	21	0	0	0	0	0	TTTCTGGTCAGGGCTCGGACA
207	21	0	0	0	0	0	TTCTGGTCAGGGCTCGGACAC
208	21	0	0	0	0	0	TCTGGTCAGGGCTCGGACACC
209	21	0	0	0	0	0	CTGGTCAGGGCTCGGACACCG
210	21	0	0	0	0	0	TGGTCAGGGCTCGGACACCGG
211	21	0	0	0	0	0	GGTCAGGGCTCGGACACCGGC
212	21	0	0	0	0	0	GTCAGGGCTCGGACACCGGCG
213	21	0	0	0	0	0	TCAGGGCTCGGACACCGGCGC
214	21	0	0	0	0	0	CAGGGCTCGGACACCGGCGCG
215	21	0	0	0	0	0	AGGGCTCGGACACCGGCGCGT
216	21	0	0	0	0	0	GGGCTCGGACACCGGCGCGTC
217	21	0	0	0	0	0	GGCTCGGACACCGGCGCGTCT
218	21	0	0	0	0	0	GCTCGGACACCGGCGCGTCTC
219	21	0	0	0	0	0	CTCGGACACCGGCGCGTCTCT
220	21	0	0	0	0	0	TCGGACACCGGCGCGTCTCTC

FIG. 24A (12)

221	21	0	0	0	0	0	CGGACACCGGCGCGTCTCTCA
222	21	0	0	0	0	0	GGACACCGGCGCGTCTCTCAA
223	21	0	0	0	0	0	GACACCGGCGCGTCTCTCAAG
224	21	0	0	0	0	0	ACACCGGCGCGTCTCTCAAGC
225	21	0	0	0	0	0	CACCGGCGCGTCTCTCAAGCT
226	21	0	0	0	0	0	ACCGGCGCGTCTCTCAAGCTC
227	21	0	0	0	0	0	CCGGCGCGTCTCTCAAGCTCG
228	21	0	0	0	0	0	CGGCGCGTCTCTCAAGCTCGC
229	21	0	0	0	0	0	GGCGCGTCTCTCAAGCTCGCC
230	21	0	0	0	0	0	GCGCGTCTCTCAAGCTCGCCT
231	21	0	0	0	0	0	CGCGTCTCTCAAGCTCGCCTC
232	21	0	0	0	0	0	GCGTCTCTCAAGCTCGCCTCT
233	21	0	0	0	0	0	CGTCTCTCAAGCTCGCCTCTT
234	21	0	0	0	0	0	GTCTCTCAAGCTCGCCTCTTC
235	21	0	0	0	0	0	TCTCTCAAGCTCGCCTCTTCG
236	21	0	0	0	0	0	CTCTCAAGCTCGCCTCTTCGG
237	21	0	0	0	0	0	TCTCAAGCTCGCCTCTTCGGA
238	21	0	0	0	0	0	CTCAAGCTCGCCTCTTCGGAG
239	21	0	0	0	0	0	TCAAGCTCGCCTCTTCGGAGC
240	21	0	0	0	0	0	CAAGCTCGCCTCTTCGGAGCT
241	21	0	0	0	0	0	AAGCTCGCCTCTTCGGAGCTG

FIG. 24A (13)

242	21	0	0	0	0	0	AGCTCGCCTCTTCGGAGCTGG
243	21	0	0	0	0	0	GCTCGCCTCTTCGGAGCTGGA
244	21	0	0	0	0	0	CTCGCCTCTTCGGAGCTGGAA
245	21	0	0	0	0	0	TCGCCTCTTCGGAGCTGGAAC
246	21	0	0	0	0	0	CGCCTCTTCGGAGCTGGAACG
247	21	0	0	0	0	0	GCCTCTTCGGAGCTGGAACGC
248	21	0	0	0	0	0	CCTCTTCGGAGCTGGAACGCC
249	21	0	0	0	0	0	CTCTTCGGAGCTGGAACGCCT
250	21	0	0	0	0	0	TCTTCGGAGCTGGAACGCCTG
251	21	0	0	0	0	0	CTTCGGAGCTGGAACGCCTGA
252	21	0	0	0	0	0	TTCGGAGCTGGAACGCCTGAT
253	21	0	0	0	0	0	TCGGAGCTGGAACGCCTGATT
254	21	0	0	0	0	0	CGGAGCTGGAACGCCTGATTG
255	21	0	0	0	0	0	GGAGCTGGAACGCCTGATTGT
256	21	0	0	0	0	0	GAGCTGGAACGCCTGATTGTC
257	21	0	0	0	0	0	AGCTGGAACGCCTGATTGTCC
258	21	0	0	0	0	0	GCTGGAACGCCTGATTGTCCC
259	21	0	0	0	0	0	CTGGAACGCCTGATTGTCCCC
260	21	0	0	0	0	0	TGGAACGCCTGATTGTCCCCA
261	21	0	0	0	0	0	GGAACGCCTGATTGTCCCCAA
262	21	0	0	0	0	0	GAACGCCTGATTGTCCCCAAC

FIG. 24A (14)

263	21	0	0	0	0	0	AACGCCTGATTGTCCCCAACA
264	21	0	0	0	0	0	ACGCCTGATTGTCCCCAACAG
265	21	0	0	0	0	0	CGCCTGATTGTCCCCAACAGC
266	21	0	0	0	0	0	GCCTGATTGTCCCCAACAGCA
267	21	0	0	0	0	0	CCTGATTGTCCCCAACAGCAA
268	21	0	0	0	0	0	CTGATTGTCCCCAACAGCAAC
269	21	0	0	0	0	0	TGATTGTCCCCAACAGCAACG
270	21	0	0	0	0	0	GATTGTCCCCAACAGCAACGG
271	21	0	0	0	0	0	ATTGTCCCCAACAGCAACGGC
272	21	0	0	0	0	0	TTGTCCCCAACAGCAACGGCG
273	21	0	0	0	0	0	TGTCCCCAACAGCAACGGCGT
274	21	0	0	0	0	0	GTCCCCAACAGCAACGGCGTG
275	21	0	0	0	0	0	TCCCCAACAGCAACGGCGTGA
276	21	0	0	0	0	0	CCCCAACAGCAACGGCGTGAT
277	21	0	0	0	0	0	CCCAACAGCAACGGCGTGATC
278	21	0	0	0	0	0	CCAACAGCAACGGCGTGATCA
279	21	0	0	0	0	0	CAACAGCAACGGCGTGATCAC
280	21	0	0	0	0	0	AACAGCAACGGCGTGATCACG
281	21	0	0	0	0	0	ACAGCAACGGCGTGATCACGA
282	21	0	0	0	0	0	CAGCAACGGCGTGATCACGAC
283	21	0	0	0	0	0	AGCAACGGCGTGATCACGACG

FIG. 24A (15)

284	21	0	0	0	0	0	GCAACGGCGTGATCACGACGA
285	21	0	0	0	0	0	CAACGGCGTGATCACGACGAC
286	21	0	0	0	0	0	AACGGCGTGATCACGACGACG
287	21	0	0	0	0	0	ACGGCGTGATCACGACGACGC
288	21	0	0	0	0	0	CGGCGTGATCACGACGACGCC
289	21	0	0	0	0	0	GGCGTGATCACGACGACGCCT
290	21	0	0	0	0	0	GCGTGATCACGACGACGCCTA
291	21	0	0	0	0	0	CGTGATCACGACGACGCCTAC
292	21	0	0	0	0	0	GTGATCACGACGACGCCTACA
293	21	0	0	0	0	0	TGATCACGACGACGCCTACAC
294	21	0	0	0	0	0	GATCACGACGACGCCTACACC
295	21	0	0	0	0	0	ATCACGACGACGCCTACACCC
296	21	0	0	0	0	0	TCACGACGACGCCTACACCCC
297	21	0	0	0	0	0	CACGACGACGCCTACACCCCC
298	21	0	0	0	0	0	ACGACGACGCCTACACCCCCG
299	21	0	0	0	0	0	CGACGACGCCTACACCCCCGG
300	21	0	0	0	0	0	GACGACGCCTACACCCCCGGG
301	21	0	0	0	0	0	ACGACGCCTACACCCCCGGGA
302	21	0	0	0	0	0	CGACGCCTACACCCCCGGGAC
303	21	0	0	0	0	0	GACGCCTACACCCCCGGGACA
304	21	0	0	0	0	0	ACGCCTACACCCCCGGGACAG

FIG. 24A (16)

305	21	0	0	0	0	0	CGCCTACACCCCCGGGACAGT
306	21	0	0	0	0	0	GCCTACACCCCCGGGACAGTA
307	21	0	0	0	0	0	CCTACACCCCCGGGACAGTAC
308	21	0	0	0	0	0	CTACACCCCCGGGACAGTACT
309	21	0	0	0	0	0	TACACCCCCGGGACAGTACTT
310	21	0	0	0	0	0	ACACCCCCGGGACAGTACTTT
311	21	0	0	0	0	0	CACCCCCGGGACAGTACTTTT
312	21	0	0	0	0	0	ACCCCCGGGACAGTACTTTTA
313	21	0	0	0	0	0	CCCCCGGGACAGTACTTTTAC
314	21	0	0	0	0	0	CCCCGGGACAGTACTTTTACC
315	21	0	0	0	0	0	CCCGGGACAGTACTTTTACCC
316	21	0	0	0	0	0	CCGGGACAGTACTTTTACCCC
317	21	0	0	0	0	0	CGGGACAGTACTTTTACCCCC
318	21	0	0	0	0	0	GGGACAGTACTTTTACCCCCG
319	21	0	0	0	0	0	GGACAGTACTTTTACCCCCGC
320	21	0	0	0	0	0	GACAGTACTTTTACCCCCGCG
321	21	0	0	0	0	0	ACAGTACTTTTACCCCCGCGG
322	21	0	0	0	0	0	CAGTACTTTTACCCCCGCGGG
323	21	0	0	0	0	0	AGTACTTTTACCCCCGCGGGG
324	21	0	0	0	0	0	GTACTTTTACCCCCGCGGGGG
325	21	0	0	0	0	0	TACTTTTACCCCCGCGGGGGT

FIG. 24A (17)

326	21	0	0	0	0	0	ACTTTTACCCCCGCGGGGGTG
327	21	0	0	0	0	0	CTTTTACCCCCGCGGGGGTGG
328	21	0	0	0	0	0	TTTTACCCCCGCGGGGGTGGC
329	21	0	0	0	0	0	TTTACCCCCGCGGGGGTGGCA
330	21	0	0	0	0	0	TTACCCCCGCGGGGGTGGCAG
331	21	0	0	0	0	0	TACCCCCGCGGGGGTGGCAGC
332	21	0	0	0	0	0	ACCCCCGCGGGGGTGGCAGCG
333	21	0	0	0	0	0	CCCCCGCGGGGGTGGCAGCGG
334	21	0	0	0	0	0	CCCCGCGGGGGTGGCAGCGGT
335	21	0	0	0	0	0	CCCGCGGGGGTGGCAGCGGTG
336	21	0	0	0	0	0	CCGCGGGGGTGGCAGCGGTGG
337	21	0	0	0	0	0	CGCGGGGGTGGCAGCGGTGGA
338	21	0	0	0	0	0	GCGGGGGTGGCAGCGGTGGAG
339	21	0	0	0	0	0	CGGGGGTGGCAGCGGTGGAGG
340	21	0	0	0	0	0	GGGGGTGGCAGCGGTGGAGGT
341	21	0	0	0	0	0	GGGGTGGCAGCGGTGGAGGTG
342	21	0	0	0	0	0	GGGTGGCAGCGGTGGAGGTGC
343	21	0	0	0	0	0	GGTGGCAGCGGTGGAGGTGCA
344	21	0	0	0	0	0	GTGGCAGCGGTGGAGGTGCAG
345	21	0	0	0	0	0	TGGCAGCGGTGGAGGTGCAGG
346	21	0	0	0	0	0	GGCAGCGGTGGAGGTGCAGGG

FIG. 24A (18)

347	21	0	0	0	0	0	GCAGCGGTGGAGGTGCAGGGG
348	21	0	0	0	0	0	CAGCGGTGGAGGTGCAGGGGG
349	21	0	0	0	0	0	AGCGGTGGAGGTGCAGGGGGC
350	21	0	0	0	0	0	GCGGTGGAGGTGCAGGGGGCG
351	21	0	0	0	0	0	CGGTGGAGGTGCAGGGGGCGC
352	21	0	0	0	0	0	GGTGGAGGTGCAGGGGGCGCA
353	21	0	0	0	0	0	GTGGAGGTGCAGGGGGCGCAG
354	21	0	0	0	0	0	TGGAGGTGCAGGGGGCGCAGG
355	21	0	0	0	0	0	GGAGGTGCAGGGGGCGCAGGG
356	21	0	0	0	0	0	GAGGTGCAGGGGGCGCAGGGG
357	21	0	0	0	0	0	AGGTGCAGGGGGCGCAGGGGG
358	21	0	0	0	0	0	GGTGCAGGGGGCGCAGGGGGC
359	21	0	0	0	0	0	GTGCAGGGGGCGCAGGGGGCG
360	21	0	0	0	0	0	TGCAGGGGGCGCAGGGGGCGG
361	21	0	0	0	0	0	GCAGGGGGCGCAGGGGGCGGC
362	21	0	0	0	0	0	CAGGGGGCGCAGGGGGCGGCG
363	21	0	0	0	0	0	AGGGGGCGCAGGGGGCGGCGT
364	21	0	0	0	0	0	GGGGGCGCAGGGGGCGGCGTC
365	21	0	0	0	0	0	GGGGCGCAGGGGGCGGCGTCA
366	21	0	0	0	0	0	GGGCGCAGGGGGCGGCGTCAC
367	21	0	0	0	0	0	GGCGCAGGGGGCGGCGTCACC

FIG. 24A (19)

368	21	0	0	0	0	0	GCGCAGGGGGCGGCGTCACCG
369	21	0	0	0	0	0	CGCAGGGGGCGGCGTCACCGA
370	21	0	0	0	0	0	GCAGGGGGCGGCGTCACCGAG
371	21	0	0	0	0	0	CAGGGGGCGGCGTCACCGAGG
372	21	0	0	0	0	0	AGGGGGCGGCGTCACCGAGGA
373	21	0	0	0	0	0	GGGGGCGGCGTCACCGAGGAG
374	21	0	0	0	0	0	GGGGCGGCGTCACCGAGGAGC
375	21	0	0	0	0	0	GGGCGGCGTCACCGAGGAGCA
376	21	0	0	0	0	0	GGCGGCGTCACCGAGGAGCAG
377	21	0	0	0	0	0	GCGGCGTCACCGAGGAGCAGG
378	21	0	0	0	0	0	CGGCGTCACCGAGGAGCAGGA
379	21	0	0	0	0	0	GGCGTCACCGAGGAGCAGGAG
380	21	0	0	0	0	0	GCGTCACCGAGGAGCAGGAGG
381	21	0	0	0	0	0	CGTCACCGAGGAGCAGGAGGG
382	21	0	0	0	0	0	GTCACCGAGGAGCAGGAGGGC
383	21	0	0	0	0	0	TCACCGAGGAGCAGGAGGGCT
384	21	0	0	0	0	0	CACCGAGGAGCAGGAGGGCTT
385	21	0	0	0	0	0	ACCGAGGAGCAGGAGGGCTTC
386	21	0	0	0	0	0	CCGAGGAGCAGGAGGGCTTCG
387	21	0	0	0	0	0	CGAGGAGCAGGAGGGCTTCGC
388	21	0	0	0	0	0	GAGGAGCAGGAGGGCTTCGCC

FIG. 24A (20)

389	21	0	0	0	0	0	AGGAGCAGGAGGGCTTCGCCG
390	21	0	0	0	0	0	GGAGCAGGAGGGCTTCGCCGA
391	21	0	0	0	0	0	GAGCAGGAGGGCTTCGCCGAC
392	21	0	0	0	0	0	AGCAGGAGGGCTTCGCCGACG
393	21	0	0	0	0	0	GCAGGAGGGCTTCGCCGACGG
394	21	0	0	0	0	0	CAGGAGGGCTTCGCCGACGGC
395	21	0	0	0	0	0	AGGAGGGCTTCGCCGACGGCT
396	21	0	0	0	0	0	GGAGGGCTTCGCCGACGGCTT
397	21	0	0	0	0	0	GAGGGCTTCGCCGACGGCTTT
398	21	0	0	0	0	0	AGGGCTTCGCCGACGGCTTTG
399	21	0	0	0	0	0	GGGCTTCGCCGACGGCTTTGT
400	21	0	0	0	0	0	GGCTTCGCCGACGGCTTTGTC
401	21	0	0	0	0	0	GCTTCGCCGACGGCTTTGTCA
402	21	0	0	0	0	0	CTTCGCCGACGGCTTTGTCAA
403	21	0	0	0	0	0	TTCGCCGACGGCTTTGTCAAA
404	21	0	0	0	0	0	TCGCCGACGGCTTTGTCAAAG
405	21	0	0	0	0	0	CGCCGACGGCTTTGTCAAAGC
406	21	0	0	0	0	0	GCCGACGGCTTTGTCAAAGCC
407	21	0	0	0	0	0	CCGACGGCTTTGTCAAAGCCC
408	21	0	0	0	0	0	CGACGGCTTTGTCAAAGCCCT
409	21	0	0	0	0	0	GACGGCTTTGTCAAAGCCCTG

FIG. 24A (21)

410	21	0	0	0	0	0	ACGGCTTTGTCAAAGCCCTGG
411	21	0	0	0	0	0	CGGCTTTGTCAAAGCCCTGGA
412	21	0	0	0	0	0	GGCTTTGTCAAAGCCCTGGAC
413	21	0	0	0	0	0	GCTTTGTCAAAGCCCTGGACG
414	21	0	0	0	0	0	CTTTGTCAAAGCCCTGGACGA
415	21	0	0	0	0	0	TTTGTCAAAGCCCTGGACGAT
416	21	0	0	0	0	0	TTGTCAAAGCCCTGGACGATC
417	21	0	0	0	0	0	TGTCAAAGCCCTGGACGATCT
418	21	0	0	0	0	0	GTCAAAGCCCTGGACGATCTG
419	21	0	0	0	0	0	TCAAAGCCCTGGACGATCTGC
420	21	0	0	0	0	0	CAAAGCCCTGGACGATCTGCA
421	21	0	0	0	0	0	AAAGCCCTGGACGATCTGCAC
422	21	0	0	0	0	0	AAGCCCTGGACGATCTGCACA
423	21	0	0	0	0	0	AGCCCTGGACGATCTGCACAA
424	21	0	0	0	0	0	GCCCTGGACGATCTGCACAAG
425	21	0	0	0	0	0	CCCTGGACGATCTGCACAAGA
426	21	0	0	0	0	0	CCTGGACGATCTGCACAAGAT
427	21	0	0	0	0	0	CTGGACGATCTGCACAAGATG
428	21	0	0	0	0	0	TGGACGATCTGCACAAGATGA
429	21	0	0	0	0	0	GGACGATCTGCACAAGATGAA
430	21	0	0	0	0	0	GACGATCTGCACAAGATGAAC

FIG. 24A (22)

431	21	0	0	0	0	0	ACGATCTGCACAAGATGAACC
432	21	0	0	0	0	0	CGATCTGCACAAGATGAACCA
433	21	0	0	0	0	0	GATCTGCACAAGATGAACCAC
434	21	0	0	0	0	0	ATCTGCACAAGATGAACCACG
435	21	0	0	0	0	0	TCTGCACAAGATGAACCACGT
436	21	0	0	0	0	0	CTGCACAAGATGAACCACGTG
437	21	0	0	0	0	0	TGCACAAGATGAACCACGTGA
438	21	0	0	0	0	0	GCACAAGATGAACCACGTGAC
439	21	0	0	0	0	0	CACAAGATGAACCACGTGACA
440	21	0	0	0	0	0	ACAAGATGAACCACGTGACAC
441	21	0	0	0	0	0	CAAGATGAACCACGTGACACC
442	21	0	0	0	0	0	AAGATGAACCACGTGACACCC
443	21	0	0	0	0	0	AGATGAACCACGTGACACCCC
444	21	0	0	0	0	0	GATGAACCACGTGACACCCCC
445	21	0	0	0	0	0	ATGAACCACGTGACACCCCCC
446	21	0	0	0	0	0	TGAACCACGTGACACCCCCCA
447	21	0	0	0	0	0	GAACCACGTGACACCCCCCAA
448	21	0	0	0	0	0	AACCACGTGACACCCCCCAAC
449	21	0	0	0	0	0	ACCACGTGACACCCCCCAACG
450	21	0	0	0	0	0	CCACGTGACACCCCCCAACGT
451	21	0	0	0	0	0	CACGTGACACCCCCCAACGTG

FIG. 24A (23)

452	21	0	0	0	0	0	ACGTGACACCCCCCAACGTGT
453	21	0	0	0	0	0	CGTGACACCCCCCAACGTGTC
454	21	0	0	0	0	0	GTGACACCCCCCAACGTGTCC
455	21	0	0	0	0	0	TGACACCCCCCAACGTGTCCC
456	21	0	0	0	0	0	GACACCCCCCAACGTGTCCCT
457	21	0	0	0	0	0	ACACCCCCCAACGTGTCCCTG
458	21	0	0	0	0	0	CACCCCCCAACGTGTCCCTGG
459	21	0	0	0	0	0	ACCCCCCAACGTGTCCCTGGG
460	21	0	0	0	0	0	CCCCCCAACGTGTCCCTGGGC
461	21	0	0	0	0	0	CCCCCAACGTGTCCCTGGGCG
462	21	0	0	0	0	0	CCCCAACGTGTCCCTGGGCGC
463	21	0	0	0	0	0	CCCAACGTGTCCCTGGGCGCT
464	21	0	0	0	0	0	CCAACGTGTCCCTGGGCGCTA
465	21	0	0	0	0	0	CAACGTGTCCCTGGGCGCTAC
466	21	0	0	0	0	0	AACGTGTCCCTGGGCGCTACC
467	21	0	0	0	0	0	ACGTGTCCCTGGGCGCTACCG
468	21	0	0	0	0	0	CGTGTCCCTGGGCGCTACCGG
469	21	0	0	0	0	0	GTGTCCCTGGGCGCTACCGGG
470	21	0	0	0	0	0	TGTCCCTGGGCGCTACCGGGG
471	21	0	0	0	0	0	GTCCCTGGGCGCTACCGGGGG
472	21	0	0	0	0	0	TCCCTGGGCGCTACCGGGGGG

FIG. 24A (24)

473	21	0	0	0	0	0	CCCTGGGCGCTACCGGGGGGC
474	21	0	0	0	0	0	CCTGGGCGCTACCGGGGGGCC
475	21	0	0	0	0	0	CTGGGCGCTACCGGGGGGCCC
476	21	0	0	0	0	0	TGGGCGCTACCGGGGGGCCCC
477	21	0	0	0	0	0	GGGCGCTACCGGGGGGCCCCC
478	21	0	0	0	0	0	GGCGCTACCGGGGGGCCCCCG
479	21	0	0	0	0	0	GCGCTACCGGGGGGCCCCCGG
480	21	0	0	0	0	0	CGCTACCGGGGGGCCCCCGGC
481	21	0	0	0	0	0	GCTACCGGGGGGCCCCCGGCT
482	21	0	0	0	0	0	CTACCGGGGGGCCCCCGGCTG
483	21	0	0	0	0	0	TACCGGGGGGCCCCCGGCTGG
484	21	0	0	0	0	0	ACCGGGGGGCCCCCGGCTGGG
485	21	0	0	0	0	0	CCGGGGGGCCCCCGGCTGGGC
486	21	0	0	0	0	0	CGGGGGGCCCCCGGCTGGGCC
487	21	0	0	0	0	0	GGGGGGCCCCCGGCTGGGCCC
488	21	0	0	0	0	0	GGGGGCCCCCGGCTGGGCCCG
489	21	0	0	0	0	0	GGGGCCCCCGGCTGGGCCCGG
490	21	0	0	0	0	0	GGGCCCCCGGCTGGGCCCGGG
491	21	0	0	0	0	0	GGCCCCCGGCTGGGCCCGGGG
492	21	0	0	0	0	0	GCCCCCGGCTGGGCCCGGGGG
493	21	0	0	0	0	0	CCCCCGGCTGGGCCCGGGGGC

FIG. 24A (25)

494	21	0	0	0	0	0	CCCCGGCTGGCCCGGGGGCG
495	21	0	0	0	0	0	CCCGGCTGGCCCGGGGGCGT
496	21	0	0	0	0	0	CCGGCTGGCCCGGGGGCGTC
497	21	0	0	0	0	0	CGGCTGGCCCGGGGGCGTCT
498	21	0	0	0	0	0	GGCTGGCCCGGGGGCGTCTA
499	21	0	0	0	0	0	GCTGGCCCGGGGGCGTCTAC
500	21	0	0	0	0	0	CTGGCCCGGGGGCGTCTACG
501	21	0	0	0	0	0	TGGCCCGGGGGCGTCTACGC
502	21	0	0	0	0	0	GGCCCGGGGGCGTCTACGCC
503	21	0	0	0	0	0	GGCCCGGGGGCGTCTACGCCG
504	21	0	0	0	0	0	GCCCGGGGGCGTCTACGCCGG
505	21	0	0	0	0	0	CCCGGGGGCGTCTACGCCGGC
506	21	0	0	0	0	0	CCGGGGGCGTCTACGCCGGCC
507	21	0	0	0	0	0	CGGGGGCGTCTACGCCGGCCC
508	21	0	0	0	0	0	GGGGGCGTCTACGCCGGCCCG
509	21	0	0	0	0	0	GGGGCGTCTACGCCGGCCCGG
510	21	0	0	0	0	0	GGGCGTCTACGCCGGCCCGGA
511	21	0	0	0	0	0	GGCGTCTACGCCGGCCCGGAG
512	21	0	0	0	0	0	GCGTCTACGCCGGCCCGGAGC
513	21	0	0	0	0	0	CGTCTACGCCGGCCCGGAGCC
514	21	0	0	0	0	0	GTCTACGCCGGCCCGGAGCCA

FIG. 24A (26)

515	21	0	0	0	0	0	TCTACGCCGGCCCGGAGCCAC
516	21	0	0	0	0	0	CTACGCCGGCCCGGAGCCACC
517	21	0	0	0	0	0	TACGCCGGCCCGGAGCCACCT
518	21	0	0	0	0	0	ACGCCGGCCCGGAGCCACCTC
519	21	0	0	0	0	0	CGCCGGCCCGGAGCCACCTCC
520	21	0	0	0	0	0	GCCGGCCCGGAGCCACCTCCC
521	21	0	0	0	0	0	CCGGCCCGGAGCCACCTCCCG
522	21	0	0	0	0	0	CGGCCCGGAGCCACCTCCCGT
523	21	0	0	0	0	0	GGCCCGGAGCCACCTCCCGTT
524	21	0	0	0	0	0	GCCCGGAGCCACCTCCCGTTT
525	21	0	0	0	0	0	CCCGGAGCCACCTCCCGTTTA
526	21	0	0	0	0	0	CCGGAGCCACCTCCCGTTTAC
527	21	0	0	0	0	0	CGGAGCCACCTCCCGTTTACA
528	21	0	0	0	0	0	GGAGCCACCTCCCGTTTACAC
529	21	0	0	0	0	0	GAGCCACCTCCCGTTTACACC
530	21	0	0	0	0	0	AGCCACCTCCCGTTTACACCA
531	21	0	0	0	0	0	GCCACCTCCCGTTTACACCAA
532	21	0	0	0	0	0	CCACCTCCCGTTTACACCAAC
533	21	0	0	0	0	0	CACCTCCCGTTTACACCAACC
534	21	0	0	0	0	0	ACCTCCCGTTTACACCAACCT
535	21	0	0	0	0	0	CCTCCCGTTTACACCAACCTC

FIG. 24A (27)

536	21	0	0	0	0	0	CTCCCGTTTACACCAACCTCA
537	21	0	0	0	0	0	TCCCGTTTACACCAACCTCAG
538	21	0	0	0	0	0	CCCGTTTACACCAACCTCAGC
539	21	0	0	0	0	0	CCGTTTACACCAACCTCAGCA
540	21	0	0	0	0	0	CGTTTACACCAACCTCAGCAG
541	21	0	0	0	0	0	GTTTACACCAACCTCAGCAGC
542	21	0	0	0	0	0	TTTACACCAACCTCAGCAGCT
543	21	0	0	0	0	0	TTACACCAACCTCAGCAGCTA
544	21	0	0	0	0	0	TACACCAACCTCAGCAGCTAC
545	21	0	0	0	0	0	ACACCAACCTCAGCAGCTACT
546	21	0	0	0	0	0	CACCAACCTCAGCAGCTACTC
547	21	0	0	0	0	0	ACCAACCTCAGCAGCTACTCC
548	21	0	0	0	0	0	CCAACCTCAGCAGCTACTCCC
549	21	0	0	0	0	0	CAACCTCAGCAGCTACTCCCC
550	21	0	0	0	0	0	AACCTCAGCAGCTACTCCCCA
551	21	0	0	0	0	0	ACCTCAGCAGCTACTCCCCAG
552	21	0	0	0	0	0	CCTCAGCAGCTACTCCCCAGC
553	21	0	0	0	0	0	CTCAGCAGCTACTCCCCAGCC
554	21	0	0	0	0	0	TCAGCAGCTACTCCCCAGCCT
555	21	0	0	0	0	0	CAGCAGCTACTCCCCAGCCTC
556	21	0	0	0	0	0	AGCAGCTACTCCCCAGCCTCT

FIG. 24A (28)

557	21	0	0	0	0	0	GCAGCTACTCCCCAGCCTCTG
558	21	0	0	0	0	0	CAGCTACTCCCCAGCCTCTGC
559	21	0	0	0	0	0	AGCTACTCCCCAGCCTCTGCG
560	21	0	0	0	0	0	GCTACTCCCCAGCCTCTGCGT
561	21	0	0	0	0	0	CTACTCCCCAGCCTCTGCGTC
562	21	0	0	0	0	0	TACTCCCCAGCCTCTGCGTCC
563	21	0	0	0	0	0	ACTCCCCAGCCTCTGCGTCCT
564	21	0	0	0	0	0	CTCCCCAGCCTCTGCGTCCTC
565	21	0	0	0	0	0	TCCCCAGCCTCTGCGTCCTCG
566	21	0	0	0	0	0	CCCCAGCCTCTGCGTCCTCGG
567	21	0	0	0	0	0	CCCAGCCTCTGCGTCCTCGGG
568	21	0	0	0	0	0	CCAGCCTCTGCGTCCTCGGGA
569	21	0	0	0	0	0	CAGCCTCTGCGTCCTCGGGAG
570	21	0	0	0	0	0	AGCCTCTGCGTCCTCGGGAGG
571	21	0	0	0	0	0	GCCTCTGCGTCCTCGGGAGGC
572	21	0	0	0	0	0	CCTCTGCGTCCTCGGGAGGCG
573	21	0	0	0	0	0	CTCTGCGTCCTCGGGAGGCGC
574	21	0	0	0	0	0	TCTGCGTCCTCGGGAGGCGCC
575	21	0	0	0	0	0	CTGCGTCCTCGGGAGGCGCCG
576	21	0	0	0	0	0	TGCGTCCTCGGGAGGCGCCGG
577	21	0	0	0	0	0	GCGTCCTCGGGAGGCGCCGGG

FIG. 24A (29)

578	21	0	0	0	0	0	CGTCCTCGGGAGGCGCCGGGG
579	21	0	0	0	0	0	GTCCTCGGGAGGCGCCGGGGC
580	21	0	0	0	0	0	TCCTCGGGAGGCGCCGGGGCT
581	21	0	0	0	0	0	CCTCGGGAGGCGCCGGGGCTG
582	21	0	0	0	0	0	CTCGGGAGGCGCCGGGGCTGC
583	21	0	0	0	0	0	TCGGGAGGCGCCGGGGCTGCC
584	21	0	0	0	0	0	CGGGAGGCGCCGGGGCTGCCG
585	21	0	0	0	0	0	GGGAGGCGCCGGGGCTGCCGT
586	21	0	0	0	0	0	GGAGGCGCCGGGGCTGCCGTC
587	21	0	0	0	0	0	GAGGCGCCGGGGCTGCCGTCG
588	21	0	0	0	0	0	AGGCGCCGGGGCTGCCGTCGG
589	21	0	0	0	0	0	GGCGCCGGGGCTGCCGTCGGG
590	21	0	0	0	0	0	GCGCCGGGGCTGCCGTCGGGA
591	21	0	0	0	0	0	CGCCGGGGCTGCCGTCGGGAC
592	21	0	0	0	0	0	GCCGGGGCTGCCGTCGGGACC
593	21	0	0	0	0	0	CCGGGGCTGCCGTCGGGACCG
594	21	0	0	0	0	0	CGGGGCTGCCGTCGGGACCGG
595	21	0	0	0	0	0	GGGGCTGCCGTCGGGACCGGG
596	21	0	0	0	0	0	GGGCTGCCGTCGGGACCGGGA
597	21	0	0	0	0	0	GGCTGCCGTCGGGACCGGGAG
598	21	0	0	0	0	0	GCTGCCGTCGGGACCGGGAGC

FIG. 24A (30)

599	21	0	0	0	0	0	CTGCCGTCGGGACCGGGAGCT
600	21	0	0	0	0	0	TGCCGTCGGGACCGGGAGCTC
601	21	0	0	0	0	0	GCCGTCGGGACCGGGAGCTCG
602	21	0	0	0	0	0	CCGTCGGGACCGGGAGCTCGT
603	21	0	0	0	0	0	CGTCGGGACCGGGAGCTCGTA
604	21	0	0	0	0	0	GTCGGGACCGGGAGCTCGTAC
605	21	0	0	0	0	0	TCGGGACCGGGAGCTCGTACC
606	21	0	0	0	0	0	CGGGACCGGGAGCTCGTACCC
607	21	0	0	0	0	0	GGGACCGGGAGCTCGTACCCG
608	21	0	0	0	0	0	GGACCGGGAGCTCGTACCCGA
609	21	0	0	0	0	0	GACCGGGAGCTCGTACCCGAC
610	21	0	0	0	0	0	ACCGGGAGCTCGTACCCGACG
611	21	0	0	0	0	0	CCGGGAGCTCGTACCCGACGA
612	21	0	0	0	0	0	CGGGAGCTCGTACCCGACGAC
613	21	0	0	0	0	0	GGGAGCTCGTACCCGACGACC
614	21	0	0	0	0	0	GGAGCTCGTACCCGACGACCA
615	21	0	0	0	0	0	GAGCTCGTACCCGACGACCAC
616	21	0	0	0	0	0	AGCTCGTACCCGACGACCACC
617	21	0	0	0	0	0	GCTCGTACCCGACGACCACCA
618	21	0	0	0	0	0	CTCGTACCCGACGACCACCAT
619	21	0	0	0	0	0	TCGTACCCGACGACCACCATC

FIG. 24A (31)

620	21	0	0	0	0	0	CGTACCCGACGACCACCATCA
621	21	0	0	0	0	0	GTACCCGACGACCACCATCAG
622	21	0	0	0	0	0	TACCCGACGACCACCATCAGC
623	21	0	0	0	0	0	ACCCGACGACCACCATCAGCT
624	21	0	0	0	0	0	CCCGACGACCACCATCAGCTA
625	21	0	0	0	0	0	CCGACGACCACCATCAGCTAC
626	21	0	0	0	0	0	CGACGACCACCATCAGCTACC
627	21	0	0	0	0	0	GACGACCACCATCAGCTACCT
628	21	0	0	0	0	0	ACGACCACCATCAGCTACCTC
629	21	0	0	0	0	0	CGACCACCATCAGCTACCTCC
630	21	0	0	0	0	0	GACCACCATCAGCTACCTCCC
631	21	0	0	0	0	0	ACCACCATCAGCTACCTCCCA
632	21	0	0	0	0	0	CCACCATCAGCTACCTCCCAC
633	21	0	0	0	0	0	CACCATCAGCTACCTCCCACA
634	21	0	0	0	0	0	ACCATCAGCTACCTCCCACAC
635	21	0	0	0	0	0	CCATCAGCTACCTCCCACACG
636	21	0	0	0	0	0	CATCAGCTACCTCCCACACGC
637	21	0	0	0	0	0	ATCAGCTACCTCCCACACGCG
638	21	0	0	0	0	0	TCAGCTACCTCCCACACGCGC
639	21	0	0	0	0	0	CAGCTACCTCCCACACGCGCC
640	21	0	0	0	0	0	AGCTACCTCCCACACGCGCCG

FIG. 24A (32)

641	21	0	0	0	0	0	GCTACCTCCCACACGCGCCGC
642	21	0	0	0	0	0	CTACCTCCCACACGCGCCGCC
643	21	0	0	0	0	0	TACCTCCCACACGCGCCGCCC
644	21	0	0	0	0	0	ACCTCCCACACGCGCCGCCCT
645	21	0	0	0	0	0	CCTCCCACACGCGCCGCCCTT
646	21	0	0	0	0	0	CTCCCACACGCGCCGCCCTTC
647	21	0	0	0	0	0	TCCCACACGCGCCGCCCTTCG
648	21	0	0	0	0	0	CCCACACGCGCCGCCCTTCGC
649	21	0	0	0	0	0	CCACACGCGCCGCCCTTCGCC
650	21	0	0	0	0	0	CACACGCGCCGCCCTTCGCCG
651	21	0	0	0	0	0	ACACGCGCCGCCCTTCGCCGG
652	21	0	0	0	0	0	CACGCGCCGCCCTTCGCCGGT
653	21	0	0	0	0	0	ACGCGCCGCCCTTCGCCGGTG
654	21	0	0	0	0	0	CGCGCCGCCCTTCGCCGGTGG
655	21	0	0	0	0	0	GCGCCGCCCTTCGCCGGTGGC
656	21	0	0	0	0	0	CGCCGCCCTTCGCCGGTGGCC
657	21	0	0	0	0	0	GCCGCCCTTCGCCGGTGGCCA
658	21	0	0	0	0	0	CCGCCCTTCGCCGGTGGCCAC
659	21	0	0	0	0	0	CGCCCTTCGCCGGTGGCCACC
660	21	0	0	0	0	0	GCCCTTCGCCGGTGGCCACCC
661	21	0	0	0	0	0	CCCTTCGCCGGTGGCCACCCG

FIG. 24A (33)

662	21	0	0	0	0	0	CCTTCGCCGGTGGCCACCCGG
663	21	0	0	0	0	0	CTTCGCCGGTGGCCACCCGGC
664	21	0	0	0	0	0	TTCGCCGGTGGCCACCCGGCG
665	21	0	0	0	0	0	TCGCCGGTGGCCACCCGGCGC
666	21	0	0	0	0	0	CGCCGGTGGCCACCCGGCGCA
667	21	0	0	0	0	0	GCCGGTGGCCACCCGGCGCAG
668	21	0	0	0	0	0	CCGGTGGCCACCCGGCGCAGC
669	21	0	0	0	0	0	CGGTGGCCACCCGGCGCAGCT
670	21	0	0	0	0	0	GGTGGCCACCCGGCGCAGCTG
671	21	0	0	0	0	0	GTGGCCACCCGGCGCAGCTGG
672	21	0	0	0	0	0	TGGCCACCCGGCGCAGCTGGG
673	21	0	0	0	0	0	GGCCACCCGGCGCAGCTGGGC
674	21	0	0	0	0	0	GCCACCCGGCGCAGCTGGGCT
675	21	0	0	0	0	0	CCACCCGGCGCAGCTGGGCTT
676	21	0	0	0	0	0	CACCCGGCGCAGCTGGGCTTG
677	21	0	0	0	0	0	ACCCGGCGCAGCTGGGCTTGG
678	21	0	0	0	0	0	CCCGGCGCAGCTGGGCTTGGG
679	21	0	0	0	0	0	CCGGCGCAGCTGGGCTTGGGC
680	21	0	0	0	0	0	CGGCGCAGCTGGGCTTGGGCC
681	21	0	0	0	0	0	GGCGCAGCTGGGCTTGGGCCG
682	21	0	0	0	0	0	GCGCAGCTGGGCTTGGGCCGC

FIG. 24A (34)

683	21	0	0	0	0	0	CGCAGCTGGGCTTGGCCGCG
684	21	0	0	0	0	0	GCAGCTGGGCTTGGCCGCGG
685	21	0	0	0	0	0	CAGCTGGGCTTGGCCGCGGC
686	21	0	0	0	0	0	AGCTGGGCTTGGCCGCGGCG
687	21	0	0	0	0	0	GCTGGGCTTGGCCGCGGCGC
688	21	0	0	0	0	0	CTGGGCTTGGCCGCGGCGCC
689	21	0	0	0	0	0	TGGGCTTGGCCGCGGCGCCT
690	21	0	0	0	0	0	GGGCTTGGCCGCGGCGCCTC
691	21	0	0	0	0	0	GGCTTGGCCGCGGCGCCTCC
692	21	0	0	0	0	0	GCTTGGCCGCGGCGCCTCCA
693	21	0	0	0	0	0	CTTGGCCGCGGCGCCTCCAC
694	21	0	0	0	0	0	TTGGCCGCGGCGCCTCCACC
695	21	0	0	0	0	0	TGGCCGCGGCGCCTCCACCT
696	21	0	0	0	0	0	GGCCGCGGCGCCTCCACCTT
697	21	0	0	0	0	0	GCCGCGGCGCCTCCACCTTC
698	21	0	0	0	0	0	CCGCGGCGCCTCCACCTTCA
699	21	0	0	0	0	0	CGCGGCGCCTCCACCTTCAA
700	21	0	0	0	0	0	GCGGCGCCTCCACCTTCAAG
701	21	0	0	0	0	0	CGGCGCCTCCACCTTCAAGG
702	21	0	0	0	0	0	GGCGCCTCCACCTTCAAGGA
703	21	0	0	0	0	0	GCGCCTCCACCTTCAAGGAG

FIG. 24A (35)

704	21	0	0	0	0	0	GCGCCTCCACCTTCAAGGAGG
705	21	0	0	0	0	0	CGCCTCCACCTTCAAGGAGGA
706	21	0	0	0	0	0	GCCTCCACCTTCAAGGAGGAA
707	21	0	0	0	0	0	CCTCCACCTTCAAGGAGGAAC
708	21	0	0	0	0	0	CTCCACCTTCAAGGAGGAACC
709	21	0	0	0	0	0	TCCACCTTCAAGGAGGAACCG
710	21	0	0	0	0	0	CCACCTTCAAGGAGGAACCGC
711	21	0	0	0	0	0	CACCTTCAAGGAGGAACCGCA
712	21	0	0	0	0	0	ACCTTCAAGGAGGAACCGCAG
713	21	0	0	0	0	0	CCTTCAAGGAGGAACCGCAGA
714	21	0	0	0	0	0	CTTCAAGGAGGAACCGCAGAC
715	21	0	0	0	0	0	TTCAAGGAGGAACCGCAGACC
716	21	0	0	0	0	0	TCAAGGAGGAACCGCAGACCG
717	21	0	0	0	0	0	CAAGGAGGAACCGCAGACCGT
718	21	0	0	0	0	0	AAGGAGGAACCGCAGACCGTG
719	21	0	0	0	0	0	AGGAGGAACCGCAGACCGTGC
720	21	0	0	0	0	0	GGAGGAACCGCAGACCGTGCC
721	21	0	0	0	0	0	GAGGAACCGCAGACCGTGCCG
722	21	0	0	0	0	0	AGGAACCGCAGACCGTGCCGG
723	21	0	0	0	0	0	GGAACCGCAGACCGTGCCGGA
724	21	0	0	0	0	0	GAACCGCAGACCGTGCCGGAG

FIG. 24A (36)

725	21	0	0	0	0	0	AACCGCAGACCGTGCCGGAGG
726	21	0	0	0	0	0	ACCGCAGACCGTGCCGGAGGC
727	21	0	0	0	0	0	CCGCAGACCGTGCCGGAGGCG
728	21	0	0	0	0	0	CGCAGACCGTGCCGGAGGCGC
729	21	0	0	0	0	0	GCAGACCGTGCCGGAGGCGCG
730	21	0	0	0	0	0	CAGACCGTGCCGGAGGCGCGC
731	21	0	0	0	0	0	AGACCGTGCCGGAGGCGCGCA
732	21	0	0	0	0	0	GACCGTGCCGGAGGCGCGCAG
733	21	0	0	0	0	0	ACCGTGCCGGAGGCGCGCAGC
734	21	0	0	0	0	0	CCGTGCCGGAGGCGCGCAGCC
735	21	0	0	0	0	0	CGTGCCGGAGGCGCGCAGCCG
736	21	0	0	0	0	0	GTGCCGGAGGCGCGCAGCCGG
737	21	0	0	0	0	0	TGCCGGAGGCGCGCAGCCGGG
738	21	0	0	0	0	0	GCCGGAGGCGCGCAGCCGGGA
739	21	0	0	0	0	0	CCGGAGGCGCGCAGCCGGGAC
740	21	0	0	0	0	0	CGGAGGCGCGCAGCCGGGACG
741	21	0	0	0	0	0	GGAGGCGCGCAGCCGGGACGC
742	21	0	0	0	0	0	GAGGCGCGCAGCCGGGACGCC
743	21	0	0	0	0	0	AGGCGCGCAGCCGGGACGCCA
744	21	0	0	0	0	0	GGCGCGCAGCCGGGACGCCAC
745	21	0	0	0	0	0	GCGCGCAGCCGGGACGCCACG

FIG. 24A (37)

746	21	0	0	0	0	0	CGCGCAGCCGGGACGCCACGC
747	21	0	0	0	0	0	GCGCAGCCGGGACGCCACGCC
748	21	0	0	0	0	0	CGCAGCCGGGACGCCACGCCG
749	21	0	0	0	0	0	GCAGCCGGGACGCCACGCCGC
750	21	0	0	0	0	0	CAGCCGGGACGCCACGCCGCC
751	21	0	0	0	0	0	AGCCGGGACGCCACGCCGCCG
752	21	0	0	0	0	0	GCCGGGACGCCACGCCGCCGG
753	21	0	0	0	0	0	CCGGGACGCCACGCCGCCGGT
754	21	0	0	0	0	0	CGGGACGCCACGCCGCCGGTG
755	21	0	0	0	0	0	GGGACGCCACGCCGCCGGTGT
756	21	0	0	0	0	0	GGACGCCACGCCGCCGGTGTC
757	21	0	0	0	0	0	GACGCCACGCCGCCGGTGTCC
758	21	0	0	0	0	0	ACGCCACGCCGCCGGTGTCCC
759	21	0	0	0	0	0	CGCCACGCCGCCGGTGTCCCC
760	21	0	0	0	0	0	GCCACGCCGCCGGTGTCCCCC
761	21	0	0	0	0	0	CCACGCCGCCGGTGTCCCCCA
762	21	0	0	0	0	0	CACGCCGCCGGTGTCCCCCAT
763	21	0	0	0	0	0	ACGCCGCCGGTGTCCCCCATC
764	21	0	0	0	0	0	CGCCGCCGGTGTCCCCCATCA
765	21	0	0	0	0	0	GCCGCCGGTGTCCCCCATCAA
766	21	0	0	0	0	0	CCGCCGGTGTCCCCCATCAAC

FIG. 24A (38)

767	21	0	0	0	0	0	CGCCGGTGTCCCCCATCAACA
768	21	0	0	0	0	0	GCCGGTGTCCCCCATCAACAT
769	21	0	0	0	0	0	CCGGTGTCCCCCATCAACATG
770	21	0	0	0	0	0	CGGTGTCCCCCATCAACATGG
771	21	0	0	0	0	0	GGTGTCCCCCATCAACATGGA
772	21	0	0	0	0	0	GTGTCCCCCATCAACATGGAA
773	21	0	0	0	0	0	TGTCCCCCATCAACATGGAAG
774	21	0	0	0	0	0	GTCCCCCATCAACATGGAAGA
775	21	0	0	0	0	0	TCCCCCATCAACATGGAAGAC
776	21	0	0	0	0	0	CCCCCATCAACATGGAAGACC
777	21	0	0	0	0	0	CCCCATCAACATGGAAGACCA
778	21	0	0	0	0	0	CCCATCAACATGGAAGACCAA
779	21	0	0	0	0	0	CCATCAACATGGAAGACCAAG
780	21	0	0	0	0	0	CATCAACATGGAAGACCAAGA
781	21	0	0	0	0	0	ATCAACATGGAAGACCAAGAG
782	21	0	0	0	0	0	TCAACATGGAAGACCAAGAGC
783	21	0	0	0	0	0	CAACATGGAAGACCAAGAGCG
784	21	0	0	0	0	0	AACATGGAAGACCAAGAGCGC
785	21	0	0	0	0	0	ACATGGAAGACCAAGAGCGCA
786	21	0	0	0	0	0	CATGGAAGACCAAGAGCGCAT
787	21	0	0	0	0	0	ATGGAAGACCAAGAGCGCATC

FIG. 24A (39)

788	21	0	0	0	0	0	TGGAAGACCAAGAGCGCATCA
789	21	0	0	0	0	0	GGAAGACCAAGAGCGCATCAA
790	21	0	0	0	0	0	GAAGACCAAGAGCGCATCAAA
791	21	0	0	0	0	0	AAGACCAAGAGCGCATCAAAG
792	21	0	0	0	0	0	AGACCAAGAGCGCATCAAAGT
793	21	0	0	0	0	0	GACCAAGAGCGCATCAAAGTG
794	21	0	0	0	0	0	ACCAAGAGCGCATCAAAGTGG
795	21	0	0	0	0	0	CCAAGAGCGCATCAAAGTGGA
796	21	0	0	0	0	0	CAAGAGCGCATCAAAGTGGAG
797	21	0	0	0	0	0	AAGAGCGCATCAAAGTGGAGC
798	21	0	0	0	0	0	AGAGCGCATCAAAGTGGAGCG
799	21	0	0	0	0	0	GAGCGCATCAAAGTGGAGCGC
800	21	0	0	0	0	0	AGCGCATCAAAGTGGAGCGCA
801	21	0	0	0	0	0	GCGCATCAAAGTGGAGCGCAA
802	21	0	0	0	0	0	CGCATCAAAGTGGAGCGCAAG
803	21	0	0	0	0	0	GCATCAAAGTGGAGCGCAAGC
804	21	0	0	0	0	0	CATCAAAGTGGAGCGCAAGCG
805	21	0	0	0	0	0	ATCAAAGTGGAGCGCAAGCGG
806	21	0	0	0	0	0	TCAAAGTGGAGCGCAAGCGGC
807	21	0	0	0	0	0	CAAAGTGGAGCGCAAGCGGCT
808	21	0	0	0	0	0	AAAGTGGAGCGCAAGCGGCTG

FIG. 24A (40)

809	21	0	0	0	0	0	AAGTGGAGCGCAAGCGGCTGC
810	21	0	0	0	0	0	AGTGGAGCGCAAGCGGCTGCG
811	21	0	0	0	0	0	GTGGAGCGCAAGCGGCTGCGG
812	21	0	0	0	0	0	TGGAGCGCAAGCGGCTGCGGA
813	21	0	0	0	0	0	GGAGCGCAAGCGGCTGCGGAA
814	21	0	0	0	0	0	GAGCGCAAGCGGCTGCGGAAC
815	21	0	0	0	0	0	AGCGCAAGCGGCTGCGGAACC
816	21	0	0	0	0	0	GCGCAAGCGGCTGCGGAACCG
817	21	0	0	0	0	0	CGCAAGCGGCTGCGGAACCGG
818	21	0	0	0	0	0	GCAAGCGGCTGCGGAACCGGC
819	21	0	0	0	0	0	CAAGCGGCTGCGGAACCGGCT
820	21	0	0	0	0	0	AAGCGGCTGCGGAACCGGCTG
821	21	0	0	0	0	0	AGCGGCTGCGGAACCGGCTGG
822	21	0	0	0	0	0	GCGGCTGCGGAACCGGCTGGC
823	21	0	0	0	0	0	CGGCTGCGGAACCGGCTGGCG
824	21	0	0	0	0	0	GGCTGCGGAACCGGCTGGCGG
825	21	0	0	0	0	0	GCTGCGGAACCGGCTGGCGGC
826	21	0	0	0	0	0	CTGCGGAACCGGCTGGCGGCC
827	21	0	0	0	0	0	TGCGGAACCGGCTGGCGGCCA
828	21	0	0	0	0	0	GCGGAACCGGCTGGCGGCCAC
829	21	0	0	0	0	0	CGGAACCGGCTGGCGGCCACC

FIG. 24A (41)

830	21	0	0	0	0	0	GGAACCGGCTGGCGGCCACCA
831	21	0	0	0	0	0	GAACCGGCTGGCGGCCACCAA
832	21	0	0	0	0	0	AACCGGCTGGCGGCCACCAAG
833	21	0	0	0	0	0	ACCGGCTGGCGGCCACCAAGT
834	21	0	0	0	0	0	CCGGCTGGCGGCCACCAAGTG
835	21	0	0	0	0	0	CGGCTGGCGGCCACCAAGTGC
836	21	0	0	0	0	0	GGCTGGCGGCCACCAAGTGCC
837	21	0	0	0	0	0	GCTGGCGGCCACCAAGTGCCG
838	21	0	0	0	0	0	CTGGCGGCCACCAAGTGCCGG
839	21	0	0	0	0	0	TGGCGGCCACCAAGTGCCGGA
840	21	0	0	0	0	0	GGCGGCCACCAAGTGCCGGAA
841	21	0	0	0	0	0	GCGGCCACCAAGTGCCGGAAG
842	21	0	0	0	0	0	CGGCCACCAAGTGCCGGAAGC
843	21	0	0	0	0	0	GGCCACCAAGTGCCGGAAGCG
844	21	0	0	0	0	0	GCCACCAAGTGCCGGAAGCGG
845	21	0	0	0	0	0	CCACCAAGTGCCGGAAGCGGA
846	21	0	0	0	0	0	CACCAAGTGCCGGAAGCGGAA
847	21	0	0	0	0	0	ACCAAGTGCCGGAAGCGGAAG
848	21	0	0	0	0	0	CCAAGTGCCGGAAGCGGAAGC
849	21	0	0	0	0	0	CAAGTGCCGGAAGCGGAAGCT
850	21	0	0	0	0	0	AAGTGCCGGAAGCGGAAGCTG

FIG. 24A (42)

851	21	0	0	0	0	0	AGTGCCGGAAGCGGAAGCTGG
852	21	0	0	0	0	0	GTGCCGGAAGCGGAAGCTGGA
853	21	0	0	0	0	0	TGCCGGAAGCGGAAGCTGGAG
854	21	0	0	0	0	0	GCCGGAAGCGGAAGCTGGAGC
855	21	0	0	0	0	0	CCGGAAGCGGAAGCTGGAGCG
856	21	0	0	0	0	0	CGGAAGCGGAAGCTGGAGCGC
857	21	0	0	0	0	0	GGAAGCGGAAGCTGGAGCGCA
858	21	0	0	0	0	0	GAAGCGGAAGCTGGAGCGCAT
859	21	0	0	0	0	0	AAGCGGAAGCTGGAGCGCATC
860	21	0	0	0	0	0	AGCGGAAGCTGGAGCGCATCG
861	21	0	0	0	0	0	GCGGAAGCTGGAGCGCATCGC
862	21	0	0	0	0	0	CGGAAGCTGGAGCGCATCGCG
863	21	0	0	0	0	0	GGAAGCTGGAGCGCATCGCGC
864	21	0	0	0	0	0	GAAGCTGGAGCGCATCGCGCG
865	21	0	0	0	0	0	AAGCTGGAGCGCATCGCGCGC
866	21	0	0	0	0	0	AGCTGGAGCGCATCGCGCGCC
867	21	0	0	0	0	0	GCTGGAGCGCATCGCGCGCCT
868	21	0	0	0	0	0	CTGGAGCGCATCGCGCGCCTG
869	21	0	0	0	0	0	TGGAGCGCATCGCGCGCCTGG
870	21	0	0	0	0	0	GGAGCGCATCGCGCGCCTGGA
871	21	0	0	0	0	0	GAGCGCATCGCGCGCCTGGAG

FIG. 24A (43)

872	21	0	0	0	0	0	AGCGCATCGCGCGCCTGGAGG
873	21	0	0	0	0	0	GCGCATCGCGCGCCTGGAGGA
874	21	0	0	0	0	0	CGCATCGCGCGCCTGGAGGAC
875	21	0	0	0	0	0	GCATCGCGCGCCTGGAGGACA
876	21	0	0	0	0	0	CATCGCGCGCCTGGAGGACAA
877	21	0	0	0	0	0	ATCGCGCGCCTGGAGGACAAG
878	21	0	0	0	0	0	TCGCGCGCCTGGAGGACAAGG
879	21	0	0	0	0	0	CGCGCGCCTGGAGGACAAGGT
880	21	0	0	0	0	0	GCGCGCCTGGAGGACAAGGTG
881	21	0	0	0	0	0	CGCGCCTGGAGGACAAGGTGA
882	21	0	0	0	0	0	GCGCCTGGAGGACAAGGTGAA
883	21	0	0	0	0	0	CGCCTGGAGGACAAGGTGAAG
884	21	0	0	0	0	0	GCCTGGAGGACAAGGTGAAGA
885	21	0	0	0	0	0	CCTGGAGGACAAGGTGAAGAC
886	21	0	0	0	0	0	CTGGAGGACAAGGTGAAGACG
887	21	0	0	0	0	0	TGGAGGACAAGGTGAAGACGC
888	21	0	0	0	0	0	GGAGGACAAGGTGAAGACGCT
889	21	0	0	0	0	0	GAGGACAAGGTGAAGACGCTC
890	21	0	0	0	0	0	AGGACAAGGTGAAGACGCTCA
891	21	0	0	0	0	0	GGACAAGGTGAAGACGCTCAA
892	21	0	0	0	0	0	GACAAGGTGAAGACGCTCAAG

FIG. 24A (44)

893	21	0	0	0	0	0	ACAAGGTGAAGACGCTCAAGG
894	21	0	0	0	0	0	CAAGGTGAAGACGCTCAAGGC
895	21	0	0	0	0	0	AAGGTGAAGACGCTCAAGGCC
896	21	0	0	0	0	0	AGGTGAAGACGCTCAAGGCCG
897	21	0	0	0	0	0	GGTGAAGACGCTCAAGGCCGA
898	21	0	0	0	0	0	GTGAAGACGCTCAAGGCCGAG
899	21	0	0	0	0	0	TGAAGACGCTCAAGGCCGAGA
900	21	0	0	0	0	0	GAAGACGCTCAAGGCCGAGAA
901	21	0	0	0	0	0	AAGACGCTCAAGGCCGAGAAC
902	21	0	0	0	0	0	AGACGCTCAAGGCCGAGAACG
903	21	0	0	0	0	0	GACGCTCAAGGCCGAGAACGC
904	21	0	0	0	0	0	ACGCTCAAGGCCGAGAACGCG
905	21	0	0	0	0	0	CGCTCAAGGCCGAGAACGCGG
906	21	0	0	0	0	0	GCTCAAGGCCGAGAACGCGGG
907	21	0	0	0	0	0	CTCAAGGCCGAGAACGCGGGG
908	21	0	0	0	0	0	TCAAGGCCGAGAACGCGGGGC
909	21	0	0	0	0	0	CAAGGCCGAGAACGCGGGGCT
910	21	0	0	0	0	0	AAGGCCGAGAACGCGGGGCTG
911	21	0	0	0	0	0	AGGCCGAGAACGCGGGGCTGT
912	21	0	0	0	0	0	GGCCGAGAACGCGGGGCTGTC
913	21	0	0	0	0	0	GCCGAGAACGCGGGGCTGTCG

FIG. 24A (45)

914	21	0	0	0	0	0	CCGAGAACGCGGGGCTGTCGA
915	21	0	0	0	0	0	CGAGAACGCGGGGCTGTCGAG
916	21	0	0	0	0	0	GAGAACGCGGGGCTGTCGAGT
917	21	0	0	0	0	0	AGAACGCGGGGCTGTCGAGTA
918	21	0	0	0	0	0	GAACGCGGGGCTGTCGAGTAC
919	21	0	0	0	0	0	AACGCGGGGCTGTCGAGTACC
920	21	0	0	0	0	0	ACGCGGGGCTGTCGAGTACCG
921	21	0	0	0	0	0	CGCGGGGCTGTCGAGTACCGC
922	21	0	0	0	0	0	GCGGGGCTGTCGAGTACCGCC
923	21	0	0	0	0	0	CGGGGCTGTCGAGTACCGCCG
924	21	0	0	0	0	0	GGGGCTGTCGAGTACCGCCGG
925	21	0	0	0	0	0	GGGCTGTCGAGTACCGCCGGC
926	21	0	0	0	0	0	GGCTGTCGAGTACCGCCGGCC
927	21	0	0	0	0	0	GCTGTCGAGTACCGCCGGCCT
928	21	0	0	0	0	0	CTGTCGAGTACCGCCGGCCTC
929	21	0	0	0	0	0	TGTCGAGTACCGCCGGCCTCC
930	21	0	0	0	0	0	GTCGAGTACCGCCGGCCTCCT
931	21	0	0	0	0	0	TCGAGTACCGCCGGCCTCCTC
932	21	0	0	0	0	0	CGAGTACCGCCGGCCTCCTCC
933	21	0	0	0	0	0	GAGTACCGCCGGCCTCCTCCG
934	21	0	0	0	0	0	AGTACCGCCGGCCTCCTCCGG

FIG. 24A (46)

935	21	0	0	0	0	0	GTACCGCCGGCCTCCTCCGGG
936	21	0	0	0	0	0	TACCGCCGGCCTCCTCCGGGA
937	21	0	0	0	0	0	ACCGCCGGCCTCCTCCGGGAG
938	21	0	0	0	0	0	CCGCCGGCCTCCTCCGGGAGC
939	21	0	0	0	0	0	CGCCGGCCTCCTCCGGGAGCA
940	21	0	0	0	0	0	GCCGGCCTCCTCCGGGAGCAG
941	21	0	0	0	0	0	CCGGCCTCCTCCGGGAGCAGG
942	21	0	0	0	0	0	CGGCCTCCTCCGGGAGCAGGT
943	21	0	0	0	0	0	GGCCTCCTCCGGGAGCAGGTG
944	21	0	0	0	0	0	GCCTCCTCCGGGAGCAGGTGG
945	21	0	0	0	0	0	CCTCCTCCGGGAGCAGGTGGC
946	21	0	0	0	0	0	CTCCTCCGGGAGCAGGTGGCC
947	21	0	0	0	0	0	TCCTCCGGGAGCAGGTGGCCC
948	21	0	0	0	0	0	CCTCCGGGAGCAGGTGGCCCA
949	21	0	0	0	0	0	CTCCGGGAGCAGGTGGCCCAG
950	21	0	0	0	0	0	TCCGGGAGCAGGTGGCCCAGC
951	21	0	0	0	0	0	CCGGGAGCAGGTGGCCCAGCT
952	21	0	0	0	0	0	CGGGAGCAGGTGGCCCAGCTC
953	21	0	0	0	0	0	GGGAGCAGGTGGCCCAGCTCA
954	21	0	0	0	0	0	GGAGCAGGTGGCCCAGCTCAA
955	21	0	0	0	0	0	GAGCAGGTGGCCCAGCTCAAA

FIG. 24A (47)

956	21	0	0	0	0	0	AGCAGGTGGCCCAGCTCAAAC
957	21	0	0	0	0	0	GCAGGTGGCCCAGCTCAAACA
958	21	0	0	0	0	0	CAGGTGGCCCAGCTCAAACAG
959	21	0	0	0	0	0	AGGTGGCCCAGCTCAAACAGA
960	21	0	0	0	0	0	GGTGGCCCAGCTCAAACAGAA
961	21	0	0	0	0	0	GTGGCCCAGCTCAAACAGAAG
962	21	0	0	0	0	0	TGGCCCAGCTCAAACAGAAGG
963	21	0	0	0	0	0	GGCCCAGCTCAAACAGAAGGT
964	21	0	0	0	0	0	GCCCAGCTCAAACAGAAGGTC
965	21	0	0	0	0	0	CCCAGCTCAAACAGAAGGTCA
966	21	0	0	0	0	0	CCAGCTCAAACAGAAGGTCAT
967	21	0	0	0	0	0	CAGCTCAAACAGAAGGTCATG
968	21	0	0	0	0	0	AGCTCAAACAGAAGGTCATGA
969	21	0	0	0	0	0	GCTCAAACAGAAGGTCATGAC
970	21	0	0	0	0	0	CTCAAACAGAAGGTCATGACC
971	21	0	0	0	0	0	TCAAACAGAAGGTCATGACCC
972	21	0	0	0	0	0	CAAACAGAAGGTCATGACCCA
973	21	0	0	0	0	0	AAACAGAAGGTCATGACCCAC
974	21	0	0	0	0	0	AACAGAAGGTCATGACCCACG
975	21	0	0	0	0	0	ACAGAAGGTCATGACCCACGT
976	21	0	0	0	0	0	CAGAAGGTCATGACCCACGTC

FIG. 24A (48)

977	21	0	0	0	0	0	AGAAGGTCATGACCCACGTCA
978	21	0	0	0	0	0	GAAGGTCATGACCCACGTCAG
979	21	0	0	0	0	0	AAGGTCATGACCCACGTCAGC
980	21	0	0	0	0	0	AGGTCATGACCCACGTCAGCA
981	21	0	0	0	0	0	GGTCATGACCCACGTCAGCAA
982	21	0	0	0	0	0	GTCATGACCCACGTCAGCAAC
983	21	0	0	0	0	0	TCATGACCCACGTCAGCAACG
984	21	0	0	0	0	0	CATGACCCACGTCAGCAACGG
985	21	0	0	0	0	0	ATGACCCACGTCAGCAACGGC
986	21	0	0	0	0	0	TGACCCACGTCAGCAACGGCT
987	21	0	0	0	0	0	GACCCACGTCAGCAACGGCTG
988	21	0	0	0	0	0	ACCCACGTCAGCAACGGCTGT
989	21	0	0	0	0	0	CCCACGTCAGCAACGGCTGTC
990	21	0	0	0	0	0	CCACGTCAGCAACGGCTGTCA
991	21	0	0	0	0	0	CACGTCAGCAACGGCTGTCAG
992	21	0	0	0	0	0	ACGTCAGCAACGGCTGTCAGC
993	21	0	0	0	0	0	CGTCAGCAACGGCTGTCAGCT
994	21	0	0	0	0	0	GTCAGCAACGGCTGTCAGCTG
995	21	0	0	0	0	0	TCAGCAACGGCTGTCAGCTGC
996	21	0	0	0	0	0	CAGCAACGGCTGTCAGCTGCT
997	21	0	0	0	0	0	AGCAACGGCTGTCAGCTGCTG

FIG. 24A (49)

998	21	0	0	0	0	0	GCAACGGCTGTCAGCTGCTGC
999	21	0	0	0	0	0	CAACGGCTGTCAGCTGCTGCT
1000	21	0	0	0	0	0	AACGGCTGTCAGCTGCTGCTT
1001	21	0	0	0	0	0	ACGGCTGTCAGCTGCTGCTTG
1002	21	0	0	0	0	0	CGGCTGTCAGCTGCTGCTTGG
1003	21	0	0	0	0	0	GGCTGTCAGCTGCTGCTTGGG
1004	21	0	0	0	0	0	GCTGTCAGCTGCTGCTTGGGG
1005	21	0	0	0	0	0	CTGTCAGCTGCTGCTTGGGGT
1006	21	0	0	0	0	0	TGTCAGCTGCTGCTTGGGGTC
1007	21	0	0	0	0	0	GTCAGCTGCTGCTTGGGGTCA
1008	21	0	0	0	0	0	TCAGCTGCTGCTTGGGGTCAA
1009	21	0	0	0	0	0	CAGCTGCTGCTTGGGGTCAAG
1010	21	0	0	0	0	0	AGCTGCTGCTTGGGGTCAAGG
1011	21	0	0	0	0	0	GCTGCTGCTTGGGGTCAAGGG
1012	21	0	0	0	0	0	CTGCTGCTTGGGGTCAAGGGA
1013	21	0	0	0	0	0	TGCTGCTTGGGGTCAAGGGAC
1014	21	0	0	0	0	0	GCTGCTTGGGGTCAAGGGACA
1015	21	0	0	0	0	0	CTGCTTGGGGTCAAGGGACAC

FIG. 24A (50)

1016	21	0	0	0	0	0	TGCTTGGGGTCAAGGGACACG
1017	21	0	0	0	0	0	GCTTGGGGTCAAGGGACACGC
1018	21	0	0	0	0	0	CTTGGGGTCAAGGGACACGCC
1019	21	0	0	0	0	0	TTGGGGTCAAGGGACACGCCT
1020	21	0	0	0	0	0	TGGGGTCAAGGGACACGCCTT
1021	21	0	0	0	0	0	GGGGTCAAGGGACACGCCTTC
1022	21	0	0	0	0	0	GGGTCAAGGGACACGCCTTCT
1023	21	0	0	0	0	0	GGTCAAGGGACACGCCTTCTG
1024	21	0	0	0	0	0	GTCAAGGGACACGCCTTCTGA

FIG. 24B (1)

```
              (Partial File -- 10 pages of 190 pages)

OligoProbe DesignStation

Probes:        C:\HITACHI\HUMBJUNX.CDS
Preparation:   C:\HITACHI\JUNMIX.PRP

       Locus pos   Tm          Locus pos   Tm            Locus pos   Tm


  atgtgcactaaaatggaacagcccttctac
     1 30    1    1    1    2    2    2    2    2    3    4
    humbjunx 1     60.76
    musbjunx 1     50.03
    muscjunx 1     30.07
    musdjunx 721   27.84
```

FIG. 24B (2)

```
tgtgcactaaaatggaacagcccttctac
     2 29    1    1    1    2    2    2    2    2    3    4
    humbjunx 65533 60.68
    musbjunx 65533 49.58
    muscjunx 1     29.97
    musdjunx 721   27.66

gtgcactaaaatggaacagcccttctac
     3 28    1    1    1    2    2    2    2    2    3    4
    humbjunx 65533 60.60
    musbjunx 65533 49.10
    muscjunx 1     29.86
    musdjunx 721   27.47
```

FIG. 24B (3)

```
tgcactaaaatggaacagcccttctacc
     4 28     1      1      1      1      2      2      2      2      3      4
    humbjunx 65533 60.60
    musbjunx 65533 46.57
    muscjunx 1     29.86
    musdjunx 729   27.47


gcactaaaatggaacagcccttctacc
     5 27     1      1      1      1      2      2      2      2      3      4
    humbjunx 5     60.51
    musbjunx 5     45.96
    muscjunx 1     29.75
    musdjunx 729   27.26
```

FIG. 24B (4)

```
cactaaaatggaacagcccttctaccac
     6 28    1     1     1     1     2     2     2     2     3     4
    humbjunx 1     60.60
    musbjunx 5     46.42
    muscjunx 1     30.79
    musdjunx 729   27.47


actaaaatggaacagcccttctaccacg
     7 28    1     1     1     1     2     2     2     3     3     4
    humbjunx 1     60.60
    musbjunx 5     46.42
    muscjunx 1     33.32
    musdjunx 729   27.47


ctaaaatggaacagcccttctaccacg
     8 27    1     1     1     1     2     2     2     3     3     4
    humbjunx 1     60.51
    musbjunx 5     45.96
    muscjunx 1     33.33
    musdjunx 729   27.26
```

FIG. 24B (5)

```
taaaatggaacagcccttctaccacgac
    9 28     1     1     1     2     2     2     2     3     3     4
   humbjunx 9      60.60
   musbjunx 5      49.10
   muscjunx 9      34.39
   musdjunx 729    27.47


aaaatggaacagcccttctaccacgac
   10 27     1     1     1     2     2     2     2     3     3     4
   humbjunx 5      60.51
   musbjunx 5      49.70
   muscjunx 9      34.44
   musdjunx 729    27.26


aaatggaacagcccttctaccacgac
   11 26     1     1     1     2     2     2     2     3     3     4
   humbjunx 5      60.42
   musbjunx 5      49.19
   muscjunx 9      34.50
   musdjunx 729    27.04
```

FIG. 24B (6)

```
aatggaacagcccttctaccacgac
    12 25     1     1     1     2     2     2     2     3     3     4
    humbjunx 5      60.32
    musbjunx 5      48.64
    muscjunx 9      34.56
    musdjunx 737    26.80


atggaacagcccttctaccacgac
    13 24     1     1     1     2     2     2     2     4     5     6
    humbjunx 13     60.20
    musbjunx 13     48.04
    muscjunx 9      34.62
    musdjunx 1      32.46
    humdjunx 65533 30.25
    musdjunx 737    26.55
```

FIG. 24B (7)

```
tggaacagcccttctaccacgac
    14 23     1     1     1     1     2     2     2     3     5     6
    humbjunx 9       60.08
    musbjunx 9       47.39
    muscjunx 9       33.39
    musdjunx 1       31.14
    humdjunx 65533 28.83
    musdjunx 737     26.27

ggaacagcccttctaccacgacg
    15 23     1     1     1     2     2     2     2     3     5     6
    humbjunx 9       61.86
    musbjunx 9       49.17
    muscjunx 9       32.09
    musdjunx 1       29.83
    humdjunx 65533 28.53
    musdjunx 737     26.27
```

FIG. 24B (8)

```
gaacagcccttctaccacgacga
    16 23    1    1    1    1    2    2    2    2    4    8
    humbjunx 9      60.08     musdjunx 737   26.27
    musbjunx 9      47.39
    muscjunx 9      30.00
    humdjunx 65533 29.66
    musdjunx 1      27.57
    humbjunx 281    26.27
    musbjunx 281    26.27

aacagcccttctaccacgacgac
    17 23    1    1    1    1    2    2    2    2    6    8
    humbjunx 17     60.08     musdjunx 737   26.27
    musbjunx 17     47.39
    muscjunx 17     30.00
    humdjunx 5      29.66
    humbjunx 281    29.35
    musbjunx 281    29.35
    musdjunx 1      27.57
```

FIG. 24B (9)

```
acagcccttctaccacgacgact
    18 23     1     1     1     1     2     2     2     2     6     8
    humbjunx 13     60.08      musdjunx 737    26.27
    musbjunx 17     47.39
    muscjunx 17     30.00
    humdjunx 5      29.66
    humbjunx 281    29.35
    musbjunx 281    29.35
    musdjunx 1      27.57

cagcccttctaccacgacgactc
    19 23     1     1     1     2     2     2     2     2     6     7
    humbjunx 13     61.86
    musbjunx 17     49.17
    muscjunx 17     30.00
    humdjunx 5      29.66
    humbjunx 281    29.35
    musbjunx 281    29.35
    musdjunx 1      27.57
```

FIG. 24B (10)

```
agcccttctaccacgacgactca
    20 23    1    1    1    1    2    2    2    2    6    7
    humbjunx 13    60.08
    musbjunx 17    46.08
    muscjunx 17    30.00
    humdjunx 5     29.66
    humbjunx 281   29.35
    musbjunx 281   29.35
    musdjunx 1     27.57

gcccttctaccacgacgactcat
    21 23    1    1    1    1    2    2    2    2    6    7
    humbjunx 21    60.08
    musbjunx 17    44.78
    muscjunx 17    30.00
    humdjunx 5     29.66
    humbjunx 281   29.35
    musbjunx 281   29.35
    musdjunx 9     27.57
```

FIG. 24B (11)

```
cccttctaccacgacgactcatac
    22 24    1     1     1     1     1     2     2     2     6     7
    humbjunx 17     60.20
    musbjunx 17     43.66
    humbjunx 281    31.67
    muscjunx 17     30.13
    humdjunx 5      29.80
    musbjunx 281    29.50
    musdjunx 5      24.84

ccttctaccacgacgactcatacac
    23 25    1     1     1     1     1     2     2     3     5     6
    humbjunx 17     60.32
    musbjunx 17     40.56
    humbjunx 289    35.76
    muscjunx 17     30.24
    musbjunx 289    29.64
    humdjunx 5      27.08
```

FIG. 24B (12)

```
cttctaccacgacgactcatacacag
    24 26     1     1     1     1     2     2     2     3     4     4
    humbjunx 17     60.42
    musbjunx 17     44.00
    humbjunx 289    35.65
    musbjunx 289    29.77


ttctaccacgacgactcatacacagc
    25 26     1     1     1     1     2     2     2     3     4     4
    humbjunx 25     60.42
    musbjunx 25     46.73
    humbjunx 289    35.65
    musbjunx 289    29.77


tctaccacgacgactcatacacagc
    26 25     1     1     1     1     2     2     2     3     4     4
    humbjunx 21     60.32
    musbjunx 25     46.08
    humbjunx 289    35.76
    musbjunx 289    29.64
```

FIG. 24B (13)

```
ctaccacgacgactcatacacagc
    27 24     1     1     1     1     2     2     2     3     4     4
    humbjunx 21    60.20
    musbjunx 25    45.37
    humbjunx 289   35.87
    musbjunx 289   29.50


taccacgacgactcatacacagctac
    28 26     1     1     1     1     1     2     2     3     4     4
    humbjunx 21    60.42
    musbjunx 25    42.26
    humbjunx 289   35.65
    musbjunx 289   29.77


accacgacgactcatacacagctac
    29 25     1     1     1     1     1     2     2     3     4     4
    humbjunx 29    60.32
    musbjunx 25    42.64
    humbjunx 289   35.76
    musbjunx 289   29.64
```

FIG. 24B (14)

```
ccacgacgactcatacacagctac
    30 24     1     1     1     1     1     2     2     3     4     4
    humbjunx 25      60.20
    musbjunx 25      43.04
    humbjunx 289     35.87
    musbjunx 289     29.50


cacgacgactcatacacagctacg
    31 24     1     1     1     1     1     2     2     3     4     5
    humbjunx 25      60.20
    musbjunx 25      43.04
    humbjunx 297     35.87
    musbjunx 297     29.50
    humdjunx 573     26.55


acgacgactcatacacagctacgg
    32 24     1     1     1     1     1     2     2     3     3     5
    humbjunx 25      60.20
    musbjunx 25      42.70
    humbjunx 293     32.92
    humdjunx 573     26.55
    musbjunx 293     26.55
```

FIG. 24B (15)

```
cgacgactcatacacagctacgg
    33 23     1     1     1     1     1     2     2     2     2     3
    humbjunx 33     60.08
    musbjunx 33     41.82
    humdjunx 573    26.27


gacgactcatacacagctacggg
    34 23     1     1     1     1     1     2     2     2     2     3
    humbjunx 29     60.08
    musbjunx 29     41.82
    humdjunx 581    26.27


acgactcatacacagctacgggatac
    35 26     1     1     1     1     2     2     2     2     2     3
    humbjunx 29     60.42
    musbjunx 29     44.26
    humdjunx 581    27.04
```

FIG. 24B (16)

```
cgactcatacacagctacgggatac
    36 25     1     1     1     1     1     2     2     2     2     3
    humbjunx 29     60.32
    musbjunx 29     43.52
    humdjunx 581    26.80


gactcatacacagctacgggatacg
    37 25     1     1     1     1     1     2     2     2     2     3
    humbjunx 37     60.32
    musbjunx 37     43.52
    humdjunx 581    26.80


actcatacacagctacgggatacgg
    38 25     1     1     1     1     1     2     2     2     2     3
    humbjunx 33     60.32
    musbjunx 37     43.52
    humdjunx 581    26.80
```

FIG. 24B (17)

```
ctcatacacagctacgggatacgg
    39 24     1     1     1     1     1     2     2     2     2     3
    humbjunx 33     60.20
    musbjunx 37     42.70
    humdjunx 581    26.55


tcatacacagctacgggatacggc
    40 24     1     1     1     1     1     1     2     2     2     3
    humbjunx 33     60.20
    musbjunx 37     39.75
    humdjunx 581    26.55


catacacagctacgggatacggc
    41 23     1     1     1     1     1     1     2     2     2     3
    humbjunx 41     60.08
    musbjunx 37     38.91
    humdjunx 581    26.27
```

FIG. 24B (18)

```
atacacagctacgggatacggcc
    42 23     1     1     1     1     1     1     2     2     2     3
    humbjunx 37      60.08
    musbjunx 37      38.91
    humdjunx 589     26.27


tacacagctacgggatacggccg
    43 23     1     1     1     1     1     2     2     2     2     3
    humbjunx 37      61.86
    musbjunx 37      41.82
    humdjunx 589     26.27


acacagctacgggatacggccg
    44 22     1     1     1     1     1     2     2     2     2     3
    humbjunx 37      61.81
    musbjunx 37      40.86
    humdjunx 589     25.96
```

FIG. 24B (19)

```
cacagctacgggatacggccg
    45 21     1     1     1     1     1     2     2     2     2     3
    humbjunx 45     61.76
    musbjunx 45     40.00
    humdjunx 589    25.62


acagctacgggatacggccgg
    46 21     1     1     1     1     1     2     2     2     2     3
    humbjunx 41     61.76
    musbjunx 45     43.38
    humdjunx 589    25.62
```

FIG. 24B (20)

```
cagctacgggatacggccgg
    47 20     1    1    1    1    1    2    2    2    2    3
    humbjunx 41     61.70
    musbjunx 45     43.90
    humdjunx 589    25.25


agctacgggatacggccggg
    48 20     1    1    1    1    1    2    2    2    3    3
    humbjunx 41     61.70
    musbjunx 45     40.35
    muscjunx 561    31.40
```

FIG. 25

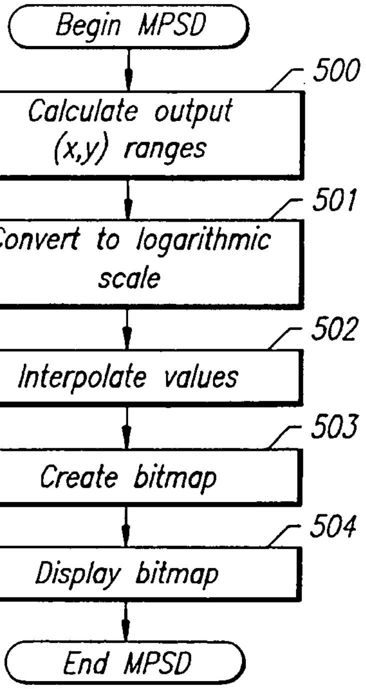

Begin MPSD
500
Calculate output (x,y) ranges
501
Convert to logarithmic scale
502
Interpolate values
503
Create bitmap
504
Display bitmap
End MPSD

FIG. 26

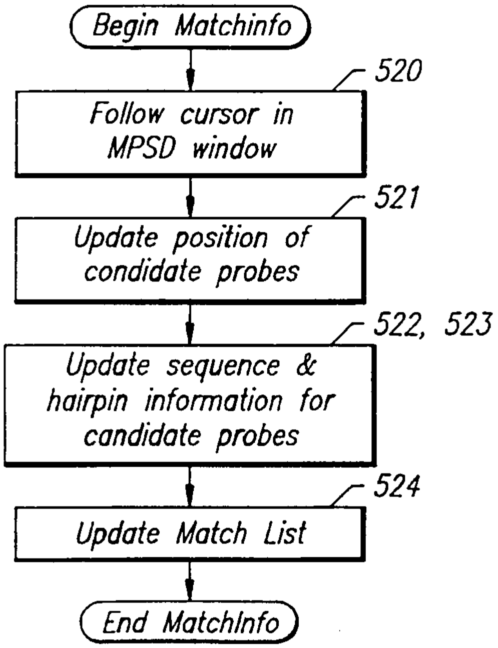

Begin Matchinfo
520
Follow cursor in MPSD window
521
Update position of condidate probes
522, 523
Update sequence & hairpin information for candidate probes
524
Update Match List
End MatchInfo

FIG. 27

```
LOCUS       HUMBJUNX     1044 bp    DNA                         19-DEC-1991
BASE COUNT        195 A    368 C    340 G    141 T
ORIGIN
        1 ATGTGCACTA AAATGGAACA GCCCTTCTAC CACGACGACT CATACACAGC TACGGGATAC
       61 GGCCGGGCCC CTGGTGGCCT CTCTCTACAC GACTACAAAC TCCTGAAACC GAGCCTGGCG
      121 GTCAACCTGG CCGACCCCTA CCGGAGTCTC AAAGCGCCTG GGGCTCGCGG ACCCGGCCCA
      181 GAGGGCGGCG GTGGCGGCAG CTACTTTTCT GGTCAGGGCT CGGACACCGG CGCGTCTCTC
      241 AAGCTCGCCT CTTCGGAGCT GGAACGCCTG ATTGTCCCCA ACAGCAACGG CGTGATCACG
      301 ACGACGCCTA CACCCCCGGG ACAGTACTTT TACCCCCGCG GGGGTGGCAG CGGTGGAGGT
      361 GCAGGGGGCG CAGGGGGCGG CGTCACCGAG GAGCAGGAGG GCTTCGCCGA CGGCTTTGTC
      421 AAAGCCCTGG ACGATCTGCA CAAGATGAAC CACGTGACAC CCCCCAACGT GTCCCTGGGC
      481 GCTACCGGGG GGCCCCCGGC TGGGCCCGGG GGCGTCTACG CCGGCCCGGA GCCACCTCCC
      541 GTTTACACCA ACCTCAGCAG CTACTCCCCA GCCTCTGCGT CCTCGGGAGG CGCCGGGGCT
      601 GCCGTCGGGA CCGGGAGCTC GTACCCGACG ACCACCATCA GCTACCTCCC ACACGCGCCG
      661 CCCTTCGCCG GTGGCCACCC GGCGCAGCTG GGCTTGGGCC GCGGCGCCTC CACCTTCAAG
      721 GAGGAACCGC AGACCGTGCC GGAGGCGCGC AGCCGGGACG CCACGCCGCC GGTGTCCCCC
      781 ATCAACATGG AAGACCAAGA GCGCATCAAA GTGGAGCGCA AGCGGCTGCG GAACCGGCTG
      841 GCGGCCACCA AGTGCCGGAA GCGGAAGCTG GAGCGCATCG CGCGCCTGGA GGACAAGGTG
      901 AAGACGCTCA AGGCCGAGAA CGCGGGGCTG TCGAGTACCG CCGGCCTCCT CCGGGAGCAG
      961 GTGGCCCAGC TCAAACAGAA GGTCATGACC CACGTCAGCA ACGGCTGTCA GCTGCTGCTT
     1021 GGGGTCAAGG GACACGCCTT CTGA
//
```

FIG. 28 (1)

```
LOCUS       HUMBJUNX      1044 bp    DNA                    19-DEC-1991
BASE COUNT       195 A    368 C    340 G    141 T
ORIGIN
        1 ATGTGCACTA AAATGGAACA GCCCTTCTAC CACGACGACT CATACACAGC TACGGGATAC
       61 GGCCGGGCCC CTGGTGGCCT CTCTCTACAC GACTACAAAC TCCTGAAACC GAGCCTGGCG
      121 GTCAACCTGG CCGACCCCTA CCGGAGTCTC AAAGCGCCTG GGGCTCGCGG ACCCGGCCCA
      181 GAGGGCGGCG GTGGCGGCAG CTACTTTTCT GGTCAGGGCT CGGACACCGG CGCGTCTCTC
      241 AAGCTCGCCT CTTCGGAGCT GGAACGCCTG ATTGTCCCCA ACAGCAACGG CGTGATCACG
      301 ACGACGCCTA CACCCCCGGG ACAGTACTTT TACCCCCGCG GGGGTGGCAG CGGTGGAGGT
      361 GCAGGGGGCG CAGGGGGCGG CGTCACCGAG GAGCAGGAGG GCTTCGCCGA CGGCTTTGTC
      421 AAAGCCCTGG ACGATCTGCA CAAGATGAAC CACGTGACAC CCCCCAACGT GTCCCTGGGC
      481 GCTACCGGGG GGCCCCCGGC TGGGCCCGGG GGCGTCTACG CCGGCCCGGA GCCACCTCCC
      541 GTTTACACCA ACCTCAGCAG CTACTCCCCA GCCTCTGCGT CCTCGGGAGG CGCCGGGGCT
      601 GCCGTCGGGA CCGGGAGCTC GTACCCGACG ACCACCATCA GCTACCTCCC ACACGCGCCG
      661 CCCTTCGCCG GTGGCCACCC GGCGCAGCTG GGCTTGGGCC GCGGCGCCTC CACCTTCAAG
      721 GAGGAACCGC AGACCGTGCC GGAGGCGCGC AGCCGGGACG CCACGCCGCC GGTGTCCCCC
      781 ATCAACATGG AAGACCAAGA GCGCATCAAA GTGGAGCGCA AGCGGCTGCG GAACCGGCTG
      841 GCGGCCACCA AGTGCCGGAA GCGGAAGCTG GAGCGCATCG CGCGCCTGGA GGACAAGGTG
      901 AAGACGCTCA AGGCCGAGAA CGCGGGGCTG TCGAGTACCG CCGGCCTCCT CCGGGAGCAG
      961 GTGGCCCAGC TCAAACAGAA GGTCATGACC CACGTCAGCA ACGGCTGTCA GCTGCTGCTT
     1021 GGGGTCAAGG GACACGCCTT CTGA
//
```

FIG. 28 (2)

```
LOCUS       HUMCJUNX      996 bp   DNA                       19-DEC-1991
BASE COUNT       226 A    342 C    299 G    129 T
ORIGIN
        1 ATGACTGCAA AGATGGAAAC GACCTTCTAT GACGATGCCC TCAACGCCTC GTTCCTCCCG
       61 TCCGAGAGCG GACCTTATGG CTACAGTAAC CCCAAGATCC TGAAACAGAG CATGACCCTG
      121 AACCTGGCCG ACCCAGTGGG GAGCCTGAAG CCGCACCTCC GCGCCAAGAA CTCGGACCTC
      181 CTCACCTCGC CCGACGTGGG GCTGCTCAAG CTGGCGTCGC CCGAGCTGGA GCGCCTGATA
      241 ATCCAGTCCA GCAACGGGCA CATCACCACC ACGCCGACCC CCACCCAGTT CCTGTGCCCC
      301 AAGAACGTGA CAGATGAGCA GGAGGGGTTC GCCGAGGGCT TCGTGCGCGC CCTGGCCGAA
      361 CTGCACAGCC AGAACACGCT GCCCAGCGTC ACGTCGGCGG CGCAGCCGGT CAACGGGGCA
      421 GGCATGGTGG CTCCCGCGGT AGCCTCGGTG GCAGGGGGCA GCGGCAGCGG CGGCTTCAGC
      481 GCCAGCCTGC ACAGCGAGCC GCCGGTCTAC GCAAACCTCA GCAACTTCAA CCCAGGCGCG
      541 CTGAGCAGCG GCGGCGGGGC GCCCTCCTAC GGCGCGGCCG GCCTGGCCTT TCCCGCGCAA
      601 CCCCAGCAGC AGCAGCAGCC GCCGCACCAC CTGCCCCAGC AGATGCCCGT GCAGCACCCG
      661 CGGCTGCAGG CCCTGAAGGA GGAGCCTCAG ACAGTGCCCG AGATGCCCGG CGAGACACCG
      721 CCCCTGTCCC CCATCGACAT GGAGTCCCAG GAGCGGATCA AGGCGGAGAG GAAGCGCATG
      781 AGGAACCGCA TCGCTGCCTC CAAGTGCCGA AAAAGGAAGC TGGAGAGAAT CGCCCGGCTG
      841 GAGGAAAAAG TGAAAACCTT GAAAGCTCAG AACTCGGAGC TGGCGTCCAC GGCCAACATG
      901 CTCAGGGAAC AGGTGGCACA GCTTAAACAG AAAGTCATGA ACCACGTTAA CAGTGGGTGC
      961 CAACTCATGC TAACGCAGCA GTTGCAAACA TTTTGA
//
```

FIG. 28 (3)

```
LOCUS       HUMDJUNX     1044 bp ss-mRNA            PRI       24-MAY-1991
DEFINITION  Human junD mRNA
ACCESSION   X56681
KEYWORDS    jun-D gene; oncogene.
SOURCE      Homo sapiens RNA.
  ORGANISM  Homo sapiens
            Eukaryota; Animalia; Metazoa; Chordata; Vertebrata; Mammalia;
            Theria; Eutheria; Primates; Haplorhini; Catarrhini; Hominidae.
REFERENCE   1  (bases 1 to 1891)
  AUTHORS   Shaul,Y.
  JOURNAL   Unpublished (1990)
  STANDARD  full automatic
REFERENCE   2  (sites)
```

FIG. 28 (4)

```
  AUTHORS   Berger,I. and Shaul,Y.
  TITLE     Structure and function of human jun-D
  JOURNAL   Unpublished (1990)
  STANDARD  full staff_review
COMMENT     From EMBL 26   entry HSJUNDR;  dated 18-MAR-1991.
FEATURES             Location/Qualifiers
     mRNA            1..1891
                     /gene="junD"
                     /evidence=EXPERIMENTAL
     CDS             175..1218
                     /product="junD protein"
                     /gene="junD"
                     /codon_start=1
     polyA_site      1891..1891
```

FIG. 28 (5)

```
BASE COUNT        162 A    405 C    360 G    117 T
ORIGIN
        1 ATGGAAACAC CCTTCTACGG CGATGAGGCG CTGAGCGGCC TGGGCGGCGG CGCCAGTGGC
       61 AGCGGCGGCA CGTTCGCGTC CCCGGGCCGC TTGTTCCCCG GGGCGCCCCC GACGGCCGCG
      121 GCCGGCAGCA TGATGAAGAA GGACGCGCTG ACGCTGAGCC TGAGTGAGCA GGTGGCGGCA
      181 GCGCTCAAGC CTGCGCCCGC GCCCGCCTCC TACCCCCCTG CCGCCGACGG CGCCCCCAGC
      241 GCGGCACCCC CCGACGGCCT GCTCGCCTCT CCCGACCTGG GGCTGCTGAA GCTGGCCTCC
      301 CCCGAGCTCG AGCGCCTCAT CATCCAGTCC AACGGGCTGG TCACCACCAC GCCGACGAGC
      361 TCACAGTTCC TCTACCCCAA GGTGGCGGCC AGCGAGGAGC AGGAGTTCGC CGAGGGCTTC
      421 GTCAAGGCCC TGGAGGATTT ACACAAGCAG AACCAGCTCG GCGCGGGCCG GGCCGCTGCC
      481 GCCGCCGCCG CCGCCGCCGG GGGGCCCTCG GGCACGGCCA CGGGCTCCGC GCCCCCCGGC
      541 GAGCTGGCCC CGGCGGCGGC CGCGCCCGAA GCGCCTGTCT ACGCGAACCT GAGCAGCTAC
      601 GCGGGCGGCG CCGGGGGCGC GGGGGGCGCC GCGACGGTCG CCTTCGCTGC CGAACCTGTG
      661 CCCTTCCCGC CGCCGCCACC CCCAGGCGCG TTGGGGCCGC CGCGCCTGGC TGCGCTCAAG
      721 GACGAGCCAC AGACGGTGCC CGACGTGCCG AGCTTCGGCG AGAGCCCGCC GTTGTCGCCC
      781 ATCGACATGG ACACGCAGGA GCGCATCAAG GCGGAGCGCA AGCGGCTGCG CAACCGCATC
      841 GCCGCCTCCA AGTGCCGCAA GCGCAAGCTG GAGCGCATCT CGCGCCTGGA AGAGAAAGTG
      901 AAGACCCTCA AGAGTCAGAA CACGGAGCTG GCGTCCACGG CGAGCCTGCT GCGCGAGCAG
      961 GTGGCGCAGC TCAAGCAGAA AGTCCTCAGC CACGTCAACA GCGGCTGCCA GCTGCTGCCC
     1021 CAGCACCAGG TCCCGGCGTA CTGA
//
```

FIG. 28 (6)

```
LOCUS       MUSBJUNX     1035 bp    DNA                     19-DEC-1991
BASE COUNT       210 A    333 C    333 G    159 T
ORIGIN
        1 ATGTGCACGA AAATGGAACA GCCTTTCTAT CACGACGACT CTTACGCAGC GGCGGGATAC
       61 GGTCGGAGCC CTGGCAGCCT GTCTCTACAC GACTACAAAC TCCTGAAACC CACCTTGGCG
      121 CTCAACCTGG CGGATCCCTA TCGGGGTCTC AAGGGTCCTG GGGCGCGGGG TCCAGGCCCG
      181 GAGGGCAGTG GGGCAGGCAG CTACTTTTCG GGTCAGGGAT CAGACACAGG CGCATCTCTG
      241 AAGCTAGCCT CCACGGAACT GGAGCGCTTG ATCGTCCCCA ACAGCAACGG CGTGATCACG
      301 ACGACGCCCA CGCCTCCGGG ACAGTACTTT TACCCCCGTG GGGGTGGCAG CGGTGGAGGT
      361 ACAGGGGGCG GCGTCACCGA GGAGCAGGAG GGCTTTGCGG ACGGTTTTGT CAAAGCCCTG
      421 GACGACCTGC ACAAGATGAA CCACGTGACG CCCCCCAACG TGTCCCTGGG CGCCAGCGGG
      481 GGTCCCCAGG CCGGCCCAGG GGGCGTCTAT GCTGGTCCGG AGCCGCCTCC CGTCTACACC
      541 AACCTCAGCA GTTACTCTCC AGCCTCTGCA CCCTCTGGAG GCTCCGGGAC CGCCGTCGGG
      601 ACTGGGAGCT CATACCCGAC GGCCACCATC AGCTACCTCC CACATGCACC ACCCTTTGCG
      661 GGCGGCCACC CGGCACAGCT GGGTTTGAGT CGTGGCGCTT CCGCCTTTAA AGAGGAACCG
      721 CAGACCGTAC CGGAGGCACG CAGCCGCGAC GCCACGCCGC CTGTGTCCCC CATCAACATG
      781 GAAGACCAGG AGCGCATCAA AGTGGAGCGA AAGCGGCTGC GGAACAGGCT GGCGGCCACC
      841 AAGTGCCGGA AGCGGAAGCT GGAGCGCATC GCGCGCCTGG AGGACAAGGT GAAGACACTC
      901 AAGGCTGAGA ACGCGGGGCT GTCGAGTGCT GCCGGTCTCC TAAGGGAGCA AGTGGCGCAG
      961 CTCAAGCAGA AGGTCATGAC CCATGTCAGC AACGGCTGCC AGTTGCTGCT AGGGGTCAAG
     1021 GGACACGCCT TCTGA
//
```

FIG. 28 (7)

```
LOCUS       MUSCJUNX     1005 bp    DNA                          19-DEC-1991
BASE COUNT       223 A    334 C    300 G    148 T
ORIGIN
        1 ATGACTGCAA AGATGGAAAC GACCTTCTAC GACGATGCCC TCAACGCCTC GTTCCTCCAG
       61 TCCGAGAGCG GTGCCTACGG CTACAGTAAC CCTAAGATCC TAAAACAGAG CATGACCTTG
      121 AACCTGGCCG ACCCGGTGGG CAGTCTGAAG CCGCACCTCC GCGCCAAGAA CTCGGACCTT
      181 CTCACGTCGC CCGACGTCGG GCTGCTCAAG CTGGCGTCGC CGGAGCTGGA GCGCCTGATC
      241 ATCCAGTCCA GCAATGGGCA CATCACCACT ACACCGACCC CCACCCAGTT CTTGTGCCCC
      301 AAGAACGTGA CCGACGAGCA GGAGGGCTTC GCCGAGGGCT TCGTGCGCGC CCTGGCTGAA
      361 CTGCATAGCC AGAACACGCT TCCCAGTGTC ACCTCCGCGG CACAGCCGGT CAGCGGGGCG
      421 GGCATGGTGG CTCCCGCGGT GGCCTCAGTA GCAGGCGCTG GCGGCGGTGG TGGCTACAGC
      481 GCCAGCCTGC ACAGTGAGCC TCCGGTCTAC GCCAACCTCA GCAACTTCAA CCCGGGTGCG
      541 CTGAGCAGCG GCGGTGGGGC GCCCTCCTAT GGCGCGGCCG GGCTGGCCTT TCCCTCGCAG
      601 CCGCAGCAGC AGCAGCAGCC GCCTCAGCCG CCGCACCACT TGCCCCAACA GATCCCGGTG
      661 CAGCACCCGC GGCTGCAAGC CCTGAAGGAA GAGCCGCAGA CCGTGCCGGA GATGCCGGGA
      721 GAGACGCCGC CCCTGTCCCC TATCGACATG GAGTCTCAGG AGCGGATCAA GGCAGAGAGG
      781 AAGCGCATGA GGAACCGCAT TGCCGCCTCC AAGTGCCGGA AAAGGAAGCT GGAGCGGATC
      841 GCTCGGCTAG AGGAAAAAGT GAAAACCTTG AAAGCGCAAA ACTCCGAGCT GGCATCCACG
      901 GCCAACATGC TCAGGGAACA GGTGGCACAG CTTAAGCAGA AAGTCATGAA CCACGTTAAC
      961 AGTGGGTGCC AACTCATGCT AACGCAGCAG TTGCAAACGT TTTGA
//
```

FIG. 28 (8)

```
LOCUS       MUSDJUNX      1026 bp   DNA                           19-DEC-1991
BASE COUNT        172 A    382 C    343 G    129 T
ORIGIN
        1 ATGGAAACGC CCTTCTATGG CGAGGAGGCG CTGAGCGGCC TGGCTGCGGG TGCGTCGAGC
       61 GTCGCTGGTG CTACTGGGGC CCCCGGCGGT GGTGGCTTCG CGCCCCCGGG CCGCGCTTTC
      121 CCCGGGGCGC CCCCGACGAG CAGCATGCTG AAGAAAGACG CGCTGACGCT CAGCCTGGCG
      181 GAGCAGGGAG CGGCGGGATT GAAACCAGGG TCGGCCACTG CACCTTCTGC GCTGCGCCCC
      241 GACGGCGCCC CCGACGGGCT GCTGGCTTCG CCGGATCTTG GGCTGCTCAA ACTCGCGTCG
      301 CCGGAGCTGG AGAGGCTGAT CATCCAGTCC AACGGGCTGG TGACCACTAC CCCGACCAGT
      361 ACGCAGTTCC TCTACCCGAA GGTGGCAGCC AGCGAGGAGC AGGAGTTCGC CGAAGGCTTC
      421 GTCAAGGCGC TGGAGGACCT GCACAAGCAA AGCCAGCTGG GTGCGGCCAC CGCGGCCACC
      481 TCAGGGGCTC CCGCGCCTCC CGCGCCCGCC GACCTGGCCG CCACCCCCGG GGCCACGGAG
      541 ACCCCGGTCT ACGCCAACCT GAGCAGTTTC GCGGGTGGCG CCGGGCCCCC TGGGGGCGCG
      601 GCCACCGTGG CTTTCGCCGC GGAGCCAGTG CCCTTCCCGC CGCCCCCGGG CGCGCTGGGG
      661 CCGCCGCCAC CTCCGCATCC ACCGCGCCTG GCCGCGCTCA AGGACGAGCC GCAGACCGTG
      721 CCGGACGTGC CGAGCTTCGG CGACAGCCCT CCGCTGTCGC CCATCGACAT GGACACGCAA
      781 GAACGCATCA AGGCGGAGCG CAAGAGGCTG CGCAACCGCA TCGCCGCCTC CAAATGCCGC
      841 AAGCGCAAGC TGGAGCGTAT CTCGCGCCTG GAGGAGAAAG TCAAGACCCT CAAAAGCCAG
      901 AACACCGAGC TGGCGTCCAC CGCCAGCCTG CTGCGCGAGC AGGTGGCGCA GCTCAAACAG
      961 AAAGTCCTCA GCCACGTCAA CAGCGGCTGC CAGCTGCTGC CCCAGCACCA GGTCCCGGCG
     1021 TACTGA
//
```

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US93/10507

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :G06F 15/42
US CL :364/413.01
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 364/413.01; 435/6; 536/23.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

MEDLINE, CA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	GENETIC ENGINEERING NEWS, Vol. 13, No. 18, issued 15 October 1993, Potera, "Hitachi Chemical Offers Probe Design Software and Service," pages 1, 22, see entire document.	1-102
Y	NUCLEIC ACIDS RESEARCH, Vol. 18, No. 7, issued 11 April 1990, Lowe et al., "A Computer Program for Selection of Oligonucleotide Primers for Polymerase Chain Reactions," pages 1757-1761, see entire document.	1-102
Y	METHODS IN ENZYMOLOGY, Vol. 183, issued 1990, Landau et al., "Fast Alignment of DNA and Protein Sequences," pages 487-502, see entire document.	1-102

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"&" document member of the same patent family

Date of the actual completion of the international search 21 December 1993	Date of mailing of the international search report 03 FEB 1994
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